

=&gt; d que 131

L7 13610 SEA FILE=HCAPLUS ABB=ON PLU=ON DEXTRAN+NT/CT  
 L11 31790 SEA FILE=HCAPLUS ABB=ON PLU=ON "GROWTH FACTORS, ANIMAL"+OLD/CT  
 L14 24623 SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTHETIC MATERIALS AND  
 PROSTHETICS"+OLD/CT  
 L15 4540 SEA FILE=HCAPLUS ABB=ON PLU=ON BONE FORMATION/CT  
 L16 3800 SEA FILE=HCAPLUS ABB=ON PLU=ON "BONE MORPHOGENETIC PROTEINS"+  
 OLD,NT/CT  
 L17 20049 SEA FILE=HCAPLUS ABB=ON PLU=ON "DENTAL MATERIALS AND  
 APPLIANCES"+OLD/CT  
 L18 117 SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTHETIC MATERIALS AND  
 PROSTHETICS (L) MAXILLOFACIAL"/CT  
 L24 17023 SEA FILE=HCAPLUS ABB=ON PLU=ON EPIDERMAL GROWTH FACTOR/CT  
 L25 18840 SEA FILE=HCAPLUS ABB=ON PLU=ON "INSULIN-LIKE GROWTH FACTOR"+N  
 T/CT  
 L26 3481 SEA FILE=HCAPLUS ABB=ON PLU=ON "FIBROBLAST GROWTH FACTOR"/CT  
 L27 21413 SEA FILE=HCAPLUS ABB=ON PLU=ON "TRANSFORMING GROWTH FACTORS"+  
 OLD,NT/CT  
 L28 8044 SEA FILE=HCAPLUS ABB=ON PLU=ON "PLATELET-DERIVED GROWTH  
 FACTORS"+OLD,NT/CT  
 L29 3800 SEA FILE=HCAPLUS ABB=ON PLU=ON "BONE MORPHOGENETIC PROTEINS"+  
 OLD,NT/CT  
 L30 51 SEA FILE=HCAPLUS ABB=ON PLU=ON ((L24 OR L25 OR L26 OR L27 OR  
 L28 OR L29) OR L11) AND L7 AND (L14 OR L15 OR L16 OR L17 OR  
 L18)  
~~L31~~ 43 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND (BONE OR DENTAL? OR  
 DENTIST? OR MANDIB? OR MAXILLOFAC? OR OSTEO?)

=&gt; d bib ab hitind 131 1-43 ;

L31 ANSWER 1 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:300930 HCAPLUS

TITLE: Improved **bone** graftINVENTOR(S): Knaack, David; Traianedes, Kathy; Diegman, Michele;  
Forsyth, Nanette; Winterbottom, John

PATENT ASSIGNEE(S): Osteotech, Inc., USA

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2003030956                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | A2   | 20030417 | WO 2002-US32941 | 20021015 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,<br>GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,<br>LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,<br>PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,<br>UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, |      |          |                 |          |

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2001-329156P P 20011012

US 2002-392462P P 20020627

AB An improved demineralized **bone** matrix (DBM) or other matrix compn. is provided that has been mixed with a stabilizing agent that acts as (1) a diffusion barrier, (2) a enzyme inhibitor, (3) a competitive substrate, or (4) a masking moiety. A diffusion barrier acts as a barrier so as to protect the **osteoinductive** factors found in DBM from being degraded by proteolytic and glycolytic enzymes at the implantation site. Stabilizing agents may be any biodegradable material such as starches, modified starches, cellulose, dextran, polymers, proteins, and collagen. As the stabilizing agents degrades or dissolves in vivo, the **osteoinductive** factors such as TGF-.beta., BMP, and IGF are activated or exposed, and the activated factors work to recruit cells from the perivascular space to the site of injury and to cause differentiation into **bone**-forming cells. The invention also provides methods of prepg., testing, and using the inventive improved **osteoinductive** matrix compns.

IC ICM A61L027-00

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 9

ST demineralized **bone** matrix graft implant TGFbeta IGF BMP

IT INDEXING IN PROGRESS

IT **Bone**  
(artificial; improved **bone** graft comprising a demineralized **bone** matrix)

IT Ceramics  
(biocompatible; improved **bone** graft comprising a demineralized **bone** matrix)

IT Transplant and Transplantation  
(**bone**; improved **bone** graft comprising a demineralized **bone** matrix)

IT Polymers  
RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(co-; improved **bone** graft comprising a demineralized **bone** matrix)

IT **Bone**  
(demineralized; improved **bone** graft comprising a demineralized **bone** matrix)

IT Polyesters  
RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(glycolide-based; improved **bone** graft comprising a demineralized **bone** matrix)

IT Proteins  
RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(growth factor-binding; improved **bone** graft comprising a demineralized **bone** matrix)

IT Alkylating agents, biological  
Antibiotics  
Antitumor agents  
**Bone formation**  
Diffusion barrier

Drug delivery systems  
 Milling (size reduction)  
 Nutrients  
 Particle size distribution  
 Stabilizing agents  
 Virus  
 Wound healing promoters  
     (improved **bone** graft comprising a demineralized **bone**  
     matrix)  
 IT Agglutinins and Lectins  
 Alkyl iodides  
 Angiogenic factors  
 Antibodies  
 Biopolymers  
     **Bone morphogenetic proteins**  
 Fatty acids  
 Lipids  
 Phosphatidylcholines  
 Polyesters  
 Polyethers  
 Polymers  
 Polysaccharides  
 Proteins  
     **Transforming growth factors**  
 RL: DEV (Device component use); TEM (Technical or engineered material  
 use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (improved **bone** graft comprising a demineralized **bone**  
     matrix)  
 IT **Growth factors, animal**  
 RL: PEP (Physical, engineering or chemical process); PYP (Physical  
 process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);  
 USES (Uses)  
     (improved **bone** graft comprising a demineralized **bone**  
     matrix)  
 IT **Growth factors, animal**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (improved **bone** graft comprising a demineralized **bone**  
     matrix)  
 IT Enzymes  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (inhibitors; improved **bone** graft comprising a demineralized  
     **bone** matrix)  
 IT Polyesters  
 RL: DEV (Device component use); TEM (Technical or engineered material  
 use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (lactide; improved **bone** graft comprising a demineralized  
     **bone** matrix)  
 IT Sulfhydryl group  
     (modifiers; improved **bone** graft comprising a demineralized  
     **bone** matrix)  
 IT Rat  
     (muscle of; improved **bone** graft comprising a demineralized  
     **bone** matrix)  
 IT Polyethers  
 RL: DEV (Device component use); TEM (Technical or engineered material  
 use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (ortho ester group-contg.; improved **bone** graft comprising a

- demineralized **bone** matrix)
- IT **Growth factors, animal**  
 RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (osteogenins; improved **bone** graft comprising a demineralized **bone** matrix)
- IT Rabbit  
 (paravertebral space of; improved **bone** graft comprising a demineralized **bone** matrix)
- IT Collagens  
 RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (sponge; improved **bone** graft comprising a demineralized **bone** matrix)
- IT **Bone**  
 (transplant; improved **bone** graft comprising a demineralized **bone** matrix)
- IT Polycarbonates  
 RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (tyrosine; improved **bone** graft comprising a demineralized **bone** matrix)
- IT Macroglobulins  
 RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (.alpha.2-, stabilizing agent; improved **bone** graft comprising a demineralized **bone** matrix)
- IT 9005-82-7, Amylose  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (-resistant starches; improved **bone** graft comprising a demineralized **bone** matrix)
- IT 1306-06-5, Hydroxyapatite 7758-87-4, Tricalcium phosphate 7778-18-9, Calcium sulfate 10103-46-5, Calcium phosphate 13767-12-9, Tetracalcium phosphate  
 RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (ceramics; improved **bone** graft comprising a demineralized **bone** matrix)
- IT 50-01-1, Guanidine hydrochloride 64-69-7, Iodoacetic acid 74-88-4, Methyl iodide 3483-12-3, Dithiothreitol 9000-94-6, Antithrombin iii 9002-89-5, Polyvinyl alcohol 9003-16-1, polyfumalic acid 9004-34-6, Cellulose **9004-54-0**, Dextran 9005-25-8, starch 26009-03-0, Polyglycolic acid 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 34346-01-5, Lactic acid-glycolic acid copolymer **61912-98-9**, Igf 81627-83-0, Mcsf  
 RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (improved **bone** graft comprising a demineralized **bone** matrix)
- IT 147783-67-3 154039-60-8, BB 2516 162514-46-7, CT1746 169799-04-6, CGS 27023A 179545-77-8, BAY 12-9566 190648-49-8, Ro 32-3555 191406-88-9, SE205 192329-42-3, AG3340  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (improved **bone** graft comprising a demineralized **bone** matrix)
- IT 54249-88-6, Dipeptidylpeptidase iv

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors, stabilizing agents; improved **bone** graft  
comprising a demineralized **bone** matrix)

IT 9028-35-7  
RL: DEV (Device component use); TEM (Technical or engineered material  
use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(inhibitors, statins; improved **bone** graft comprising a  
demineralized **bone** matrix)

IT 9001-92-7, Proteinase 9004-08-4, Cathepsin 9032-92-2, Glycosidase  
141907-41-7  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; improved **bone** graft comprising a demineralized  
**bone** matrix)

IT 55-91-4, Diisopropylfluorophosphate 60-32-2, .epsilon.-Aminocaproic acid  
66-71-7, 1,10-Phenanthroline 67-42-5, Egta 128-53-0, N-Ethylmaleimide  
139-33-3 329-30-6, 1-Chloro-3-tosylamido-4-phenyl-2-butanone 329-98-6,  
phenylmethylsulfonyl fluoride 1670-14-0, Benzamidine hydrochloride  
2364-87-6 8001-27-2, Hirudin 9035-81-8, Trypsin inhibitor 9041-92-3,  
.alpha.1-Antitrypsin 9076-44-2, Chymostatin 9087-70-1, Aprotinin  
26305-03-3, Pepstatin a 34284-75-8, 4-(2-Aminoethyl)benzenesulfonyl  
fluoride 36357-77-4, Phosphoramidon 37691-11-5, Antipain 51798-45-9,  
Elastatinal 55123-66-5, Leupeptin 58970-76-6, Bestatin 66701-25-5,  
E-64 76684-89-4, e-64c 76808-15-6, Ebelactone b 76808-16-7,  
Ebelactone a 88321-09-9, e-64d 90614-48-5, Diprotin a 96551-81-4,  
Arphamenine A 100157-28-6, Foroxymithine 103900-19-2, Arphamenine B  
110044-82-1, Calpain inhibitor I 110115-07-6, Calpain inhibitor ii  
129085-76-3, leuhistin 134448-10-5, ca-074 141175-92-3,  
.alpha.1-Antichymotrypsin 187402-73-9, Phebestin  
RL: DEV (Device component use); TEM (Technical or engineered material  
use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(stabilizing agent; improved **bone** graft comprising a  
demineralized **bone** matrix)

L31 ANSWER 2 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:282718 HCAPLUS

DOCUMENT NUMBER: 138:282352

TITLE: Traversal of nucleic acid molecules through a tissue  
fluid space and expression in repair cells

INVENTOR(S): Sosnowski, Barbara A.; Pierce, Glenn

PATENT ASSIGNEE(S): Selective Genetics, Inc., USA

SOURCE: PCT Int. Appl., 95 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND                                                            | DATE     | APPLICATION NO. | DATE     |
|---------------|-----------------------------------------------------------------|----------|-----------------|----------|
| WO 2003029429 | A2                                                              | 20030410 | WO 2002-US31546 | 20021002 |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, |          |                 |          |
|               | CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, |          |                 |          |
|               | GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, |          |                 |          |
|               | LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, |          |                 |          |
|               | PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, |          |                 |          |
|               | UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, |          |                 |          |
|               | RU, TJ, TM                                                      |          |                 |          |

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2001-327513P P 20011003

AB Disclosed are methods for use in transferring nucleic acids into cells at a wound site assocd. with a fluid space. These gene transfer protocols are suitable for use in transferring various nucleic acids into cartilage, cardiac muscle, and other tissues, and have many uses including treating diseases such as arthritis and ischemic heart disease, and promoting wound healing. The invention further disclosed pharmaceutical compns. that may be used in the practice of the invention to transfer the nucleic acid of interest. Such compns. include any multi-partitioned biocompatible matrix in combination with multiple nucleic acids of interest. Thus, collagen collagen-immobilized fibroblast growth factor (FGF) genes induce angiogenesis in vitro, and FGF gene delivery to skeletal muscle wounds induces both angiogenesis and arteriogenesis and well as induces myocyte regeneration.

IC ICM C12N

CC 3-2 (Biochemical Genetics)

Section cross-reference(s): 1

IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (10, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (2, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (3, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (4, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (5, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (6, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (7, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (8, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (9, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

- IT **Prosthetic materials and Prosthetics**  
(bioactive glass, biocompatible; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Growth factors, animal**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(chondromodulins, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT Angiogenesis  
**Bone formation**  
Regeneration, animal  
Wound healing  
(gene therapy for stimulation of; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gene therapy with nucleic acids encoding BMP-12; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gene therapy with nucleic acids encoding BMP-13; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT Antibodies  
**Bone morphogenetic proteins**  
Growth factor receptors  
**Growth factors, animal**  
Hepatocyte growth factor  
Hormones, animal, biological studies  
Insulin-like growth factor receptors  
Interleukin 1  
Interleukin 6  
Interleukin 8  
Interleukins  
Leukemia inhibitory factor  
**Platelet-derived growth factors**  
Transcription factors  
**Transforming growth factors**  
Tumor necrosis factors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Growth factors, animal**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(skeletal growth factors, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT Adenoviral vectors  
Antiarthritics  
**Bone**  
Cartilage  
Gene therapy  
Heart  
Plasmid vectors  
Retroviral vectors  
Wound  
Wound healing promoters  
(traversal of nucleic acid mols. through a tissue fluid space and

expression in repair cells)

IT **Transforming growth factors**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.alpha.-, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT **Transforming growth factors**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.1-, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT **Transforming growth factors**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.2-, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT 1306-06-5, Hydroxyapatite 9002-84-0, Polytetrafluoroethylene 9002-88-4, Polyethylene 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-20-7, Polyvinylacetate 9004-34-6, Cellulose, biological studies **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronan 9004-67-5, Methyl cellulose 9005-32-7, Alginate acid 9012-76-4, Chitosan 9016-00-6, Poly(dimethylsiloxane) 11098-82-1, Aluminate 24937-78-8, Poly(ethylene-vinyl acetate) 25322-68-3, Polyethylene glycol 25852-47-5, Hydrogel 26100-51-6, Lactic acid polymer 26124-68-5, Glycolic acid polymer 31900-57-9, Poly(dimethylsiloxane) 34346-01-5, Lactic acid-Glycolic acid copolymer 124586-38-5, Hydrogel  
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(biocompatible; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT 9001-27-8, Blood-coagulation factor VIII 9001-28-9, Blood-coagulation factor IX 9002-64-6, Parathyroid hormone 9002-72-6, Growth hormone 11096-26-7, Erythropoietin 57285-09-3, Inhibin **61912-98-9**, Insulin-like growth factor **62031-54-3**, Fibroblast growth factor **62229-50-9**, Epidermal growth factor **67763-96-6**, Insulin-like growth factor I **67763-97-7**, Insulin-like growth factor II 81627-83-0, Macrophage-colony stimulating factor 83869-56-1, Granulocyte-macrophage-colony stimulating factor 103370-86-1, Parathyroid hormone-related peptide 106096-93-9, Basic fibroblast growth factor 114949-22-3, Activin 127464-60-2, Vascular endothelial growth factor 139639-23-9, Tissue plasminogen activator 189460-40-0, Connective tissue-growth factor 252959-51-6, Growth differentiation factor 11  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

L31 ANSWER 3 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:260864 HCAPLUS

DOCUMENT NUMBER: 138:276278

TITLE: Lipophilic-coated microparticles containing a protein drug

INVENTOR(S): Kim, Myung-Jin; Kim, Sun-Jin; Kwon, Kyu-Chan; Kim, Joon

PATENT ASSIGNEE(S): S. Korea

SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S.



Ser. No. 648,196, abandoned.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE        |
|------------------------|------|----------|-----------------|-------------|
| US 2003064105          | A1   | 20030403 | US 2002-160784  | 20020603    |
| PRIORITY APPLN. INFO.: |      |          | US 2000-648196  | B2 20000825 |

AB A solid lipophilic microparticle having an av. particle size ranging 0.1-200 .mu.m, comprises a lipophilic substance, hyaluronic acid or an inorg. salt and an active ingredient selected from the group consisting of a protein or peptide drug. The microparticle retains the full activity of the active ingredient, and when formulated in the form of an oil dispersion or an oil-in-water emulsion, it releases in an in vivo environment the active ingredient in a controlled manner over a long period. Human growth hormone (hGH) was dissolved in 5 mM PBS to a concn. of 2 mg/mL and then Tween 80 was added thereto at 0.01 wt. % based on the wt. of PBS. Sodium hyaluronate having a mol. wt. of 1,000,000 was dissolved therein to a concn. of 0.2% (w/v). The resulting soln. was provided to a spray dryer at a flow rate of 3 mL/min to obtain primary particles. In this step, the inflow air temp. was 85.degree.. The av. particle size of the primary particles thus obtained was 3 .mu.m. Lecithin was dissolved in ethanol to a concn. of 1% and then the primary particles were suspended therein at a concn. of 1%. The av. particle size of the microparticles thus obtained was 7 .mu.m.

IC ICM A61K039-395  
ICS A61K038-21; A61K038-19; A61K038-28; A61K009-16; A61K009-50; A61K045-00; C08B037-00; C07H001-00; C07G001-00; A61K038-00

NCL 424493000; 424085100; 424130100; 424085400; 514003000; 514012000; 536053000

CC 63-6 (Pharmaceuticals)

IT Albumins, biological studies  
**Bone morphogenetic proteins**  
Cod liver oil  
Corn oil  
Cottonseed oil  
Diglycerides  
Edible oils  
Fatty acids, biological studies  
Gelatins, biological studies  
Glycerides, biological studies  
Interferons  
Interleukins  
Lecithins  
Lipids, biological studies  
Monoglycerides  
Olive oil  
Paraffin oils  
Peanut oil  
Peptides, biological studies  
Phosphatidylcholines, biological studies  
Phosphatidylethanolamines, biological studies  
Phosphatidylserines  
Polyoxyalkylenes, biological studies

Proteins  
Safflower oil  
Soybean oil  
Sunflower oil  
Tumor necrosis factors

## Waxes

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(lipophilic-coated microparticles contg. protein drugs)

IT 50-70-4, Sorbitol, biological studies 50-99-7, Glucose, biological studies 56-40-6, Glycine, biological studies 56-41-7, Alanine, biological studies 56-86-0, Glutamic acid, biological studies 56-87-1, Lysine, biological studies 57-10-3, Palmitic acid, biological studies 57-11-4, Stearic acid, biological studies 57-48-7, Fructose, biological studies 57-50-1, Saccharose, biological studies 58-86-6, Xylose, biological studies 59-23-4, Galactose, biological studies 69-65-8, Mannitol 69-79-4, Maltose 74-79-3, Arginine, biological studies 99-20-7, Trehalose 111-01-3, Squalane 111-02-4, Squalene 544-63-8, Myristic acid, biological studies 1338-43-8, Sorbitan monooleate 9002-72-6, Somatotropin 9004-10-8, Insulin, biological studies **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic acid 9005-65-6, Tween 80 9007-28-7, Chondroitin sulfate 9034-39-3, Growth hormone releasing hormone 9039-53-6, Urokinase 9067-32-7, Sodium hyaluronate 11096-26-7, Erythropoietin 11099-07-3, Glyceryl stearate 25322-68-3, Polyethylene glycol 26266-57-9, Sorbitan palmitate 31799-91-4, Potassium hyaluronate 56451-84-4, Sorbitan stearate **61912-98-9**, Insulin-like growth factor **62229-50-9**, Epidermal growth factor 63660-98-0, Calcium hyaluronate 66419-50-9, Bovine growth hormone **67763-96-6**, Insulin-like growth factor I 80966-39-8, Magnesium hyaluronate 81627-83-0, Macrophage-colony stimulating factor 83869-56-1, Granulocyte macrophage-colony stimulating factor 95685-92-0, Ammonium hyaluronate 97793-28-7, Atriopeptin-III 126467-48-9, Porcine growth hormone 139639-23-9, Tissue plasminogen activator 143011-72-7, Granulocyte-colony stimulating factor 177402-92-5, Zinc hyaluronate 205069-30-3, Cobalt hyaluronate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(lipophilic-coated microparticles contg. protein drugs)

L31 ANSWER 4 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:695831 HCAPLUS

DOCUMENT NUMBER: 137:237785

TITLE: Porous beta-tricalcium phosphate granules for **bone** implantation, and methods for producing same

INVENTOR(S): Dalal, Paresh S.; Dimaano, Godofredo R.; Toth, Carol Ann; Kulkarni, Shailesh C.

PATENT ASSIGNEE(S): Stryker Corporation, USA

SOURCE: PCT Int. Appl., 151 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2002070029 | A2   | 20020912 | WO 2002-US5827  | 20020226 |

WO 2002070029 A3 20030206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003049328 A1 20030313 US 2001-798518 20010302

PRIORITY APPLN. INFO.:

US 2001-798518 A 20010302

US 2001-960789 A 20010921

AB A porous .beta.-tricalcium phosphate material for **bone** implantation is provided. The multiple pores in the porous TCP body are sep. discrete voids and are not interconnected. The pore size diam. is in the range of 20-500 .mu.m, preferably 50-125 .mu.m. The porous .beta.-TCP material provides a carrier matrix for bioactive agents and can form a moldable putty compn. upon the addn. of a binder. Preferably, the bioactive agent is encapsulated in a biodegradable agent. The invention provides a kit and an implant device comprising the porous .beta.-TCP, and a bioactive agent and a binder. The invention also provides an implementable prosthetic device comprising a prosthetic implant having a surface region, a porous .beta.-TCP material disposed on the surface region optionally comprising at least a bioactive agent or a binder. Methods of producing the porous .beta.-TCP material and including **bone** formation are also provided.

IC ICM A61L027-12

ICS A61L027-56

CC 63-7 (Pharmaceuticals)

Section cross-reference(s): 2, 15

ST **bone** implant porous beta tricalcium phosphate granule sequenceIT **Bone morphogenetic proteins**

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(2; porous .beta.-tricalcium phosphate granules for **bone** implantation)

IT **Bone morphogenetic proteins**

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(3; porous .beta.-tricalcium phosphate granules for **bone** implantation)

IT **Bone morphogenetic proteins**

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(4; porous .beta.-tricalcium phosphate granules for **bone** implantation)

IT **Bone morphogenetic proteins**

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(5; porous .beta.-tricalcium phosphate granules for **bone** implantation)

- IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(6; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(7; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Nucleic acids  
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(BMP-encoding; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Carbohydrates, biological studies  
RL: TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(aldonic acids, polymer; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Transplant and Transplantation  
(allotransplant; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Polyesters, biological studies  
RL: TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(arom.; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT **Bone**  
Hip  
(artificial; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Transplant and Transplantation  
(autotransplant; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Polymers, biological studies  
RL: TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(biodegradable; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Glues  
(fibrin-contg.; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Drug delivery systems  
(granules; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Drug delivery systems  
**Prosthetic materials and Prosthetics**  
(implants; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Putty  
(medical; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Polyethers, biological studies

RL: TEM (Technical or engineered material use); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)  
 (ortho ester group-contg.; porous .beta.-tricalcium phosphate granules  
 for **bone** implantation)

IT **Growth factors, animal**

RL: PEP (Physical, engineering or chemical process); PYP (Physical  
 process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);  
 USES (Uses)

(**osteogenins**; porous .beta.-tricalcium phosphate granules for  
**bone** implantation)

IT Polyimides, biological studies

RL: TEM (Technical or engineered material use); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)

(polyanhydride-; porous .beta.-tricalcium phosphate granules for  
**bone** implantation)

IT Polyanhydrides

RL: TEM (Technical or engineered material use); THU (Therapeutic use);  
 BIOL (Biological study); USES (Uses)

(polyimide-; porous .beta.-tricalcium phosphate granules for  
**bone** implantation)

IT Binders

Encapsulation

Granulation

Mammalia

Molecular weight distribution

Particle size distribution

Porosity

**Prosthetic materials and Prosthetics**

Protein sequences

Sieving

Sintering

Sublimation

cDNA sequences

(porous .beta.-tricalcium phosphate granules for **bone**  
 implantation)

IT Gelatins, biological studies

Glycosaminoglycans, biological studies

Mucins

Peptides, biological studies

Petrolatum

Polyamides, biological studies

Polyoxyalkylenes, biological studies

Polysaccharides, biological studies

Polyurethanes, biological studies

RL: MOA (Modifier or additive use); TEM (Technical or engineered material  
 use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(porous .beta.-tricalcium phosphate granules for **bone**  
 implantation)

IT Polyvinyl butyrals

RL: NUU (Other use, unclassified); USES (Uses)

(porous .beta.-tricalcium phosphate granules for **bone**  
 implantation)

IT **Bone morphogenetic proteins**

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP  
 (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC  
 (Process); USES (Uses)

(porous .beta.-tricalcium phosphate granules for **bone**

- implantation)
- IT Interleukin 6  
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Collagens, biological studies  
Polyanhydrides  
Polyphosphazenes  
RL: TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Drug delivery systems  
(powders; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Fats and Glyceridic oils, biological studies  
RL: MOA (Modifier or additive use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sesame; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT Drug delivery systems  
(sustained-release; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT **Transforming growth factors**  
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(.beta.-; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT 9001-78-9, Alkaline phosphatase  
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(**osteogenesis** marker; porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT 7758-87-4, .beta.-Tricalcium phosphate  
RL: DEV (Device component use); PRP (Properties); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT 69-65-8, Mannitol **9004-54-0**, Dextran, biological studies  
9004-61-9, Hyaluronic acid 9004-62-0, Hydroxyethylcellulose 9004-65-3, Hydroxypropyl methylcellulose 9005-38-3, Sodium alginate 9007-28-7, Chondroitin sulfate 9012-76-4, Chitosan 9032-42-2, Hydroxyethyl methylcellulose 9041-56-9, Hydroxybutyl methylcellulose 9050-04-8 9067-32-7, Sodium hyaluronate 9078-35-7 24991-23-9 25322-68-3, Polyethylene glycol 25513-46-6, Polyglutamic acid 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 34346-01-5 52352-27-9, Polyhydroxybutyric acid 78644-42-5, Polymalic acid 106392-12-5, Poloxamer  
RL: MOA (Modifier or additive use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(porous .beta.-tricalcium phosphate granules for **bone** implantation)
- IT 9002-89-5, Polyvinyl alcohol 9003-39-8, Polyvinylpyrrolidone

9004-36-8, Cellulose acetate butyrate 9005-25-8, Starch, uses

RL: NUU (Other use, unclassified); USES (Uses)

(porous .beta.-tricalcium phosphate granules for **bone** implantation)

IT 50-23-7, Hydrocortisone 50-28-2, Estradiol, biological studies  
57-83-0, Progesterone, biological studies 302-79-4, Retinoic acid  
1406-16-2, Vitamin d 9002-64-6, Pth 9002-72-6, Growth hormone  
9004-10-8, Insulin, biological studies **62031-54-3**, Fgf  
**67763-96-6**, Igf-i  
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(porous .beta.-tricalcium phosphate granules for **bone** implantation)

IT 9003-01-4D, Polyacrylic acid, derivs. 24937-78-8, Ethylene-vinyl acetate copolymer 24980-41-4, Poly(caprolactone) 25248-42-4, Poly(caprolactone) 26009-03-0, Polyglycolide 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26063-00-3, Polyhydroxybutyrate 26161-42-2 26202-08-4, Polyglycolide 26680-10-4, Poly(D,L-lactide) 26744-04-7 26780-50-7, Polyglactin 29223-92-5, Poly(p-dioxanone) 31852-84-3, Poly(trimethylene carbonate) 33135-50-1, Poly(L-lactide) 41706-81-4, Poly(..epsilon.-caprolactone-glycolide) 50862-75-4, Poly(oxy(1-methyl-2-oxo-1,2-ethanediyl)) 75734-93-9, Poly(glycolide-trimethylene carbonate) 129515-24-8, Poly(D,L-lactide-trimethylene carbonate)  
RL: TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(porous .beta.-tricalcium phosphate granules for **bone** implantation)

IT 458061-50-2  
RL: PRP (Properties)  
(unclaimed nucleotide sequence; porous beta-tricalcium phosphate granules for **bone** implantation, and methods for producing same)

IT 458061-41-1 458061-42-2 458061-43-3 458061-44-4 458061-45-5  
458061-46-6 458061-47-7 458061-48-8 458061-49-9  
RL: PRP (Properties)  
(unclaimed protein sequence; porous beta-tricalcium phosphate granules for **bone** implantation, and methods for producing same)

L31 ANSWER 5 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:533944 HCAPLUS

DOCUMENT NUMBER: 137:99052

TITLE: Hybrid matrix implants and explants

INVENTOR(S): Mineau-Hanschke, Rochelle

PATENT ASSIGNEE(S): Trans Karyotic Therapies, Inc., USA

SOURCE: U.S., 29 pp., Cont.-in-part of U. S. Ser. No. 312,246.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|------------|------|----------|-----------------|----------|
| US 6419920 | B1   | 20020716 | US 1999-413715  | 19991005 |
| US 5965125 | A    | 19991012 | US 1995-548002  | 19951025 |

|               |    |          |                 |          |
|---------------|----|----------|-----------------|----------|
| NZ 502455     | A  | 20010126 | NZ 1996-502455  | 19961025 |
| US 6472181    | B1 | 20021029 | US 1999-312246  | 19990514 |
| WO 2001024842 | A2 | 20010412 | WO 2000-US27362 | 20001004 |
| WO 2001024842 | A3 | 20010830 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

|               |    |          |                |          |
|---------------|----|----------|----------------|----------|
| AU 2000078545 | A5 | 20010510 | AU 2000-78545  | 20001004 |
| BR 2000014503 | A  | 20020611 | BR 2000-14503  | 20001004 |
| EP 1221937    | A2 | 20020717 | EP 2000-968669 | 20001004 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL

|               |    |          |                |          |
|---------------|----|----------|----------------|----------|
| JP 2003511100 | T2 | 20030325 | JP 2001-527841 | 20001004 |
| US 2003077260 | A1 | 20030424 | US 2002-188628 | 20020702 |

PRIORITY APPLN. INFO.:

|                 |    |          |
|-----------------|----|----------|
| US 1995-548002  | A3 | 19951025 |
| US 1999-312246  | A2 | 19990514 |
| NZ 1996-321417  |    | 19961025 |
| US 1999-413715  | A1 | 19991005 |
| US 2000-662037  | A1 | 20000914 |
| WO 2000-US27362 | W  | 20001004 |

AB A compn. has a body of matrix material made up of insol. collagen fibrils, and disposed therewithin (a) a plurality of vertebrate cells; (b) a plurality of microspheres; and (c) an agent such as a factor that promotes vascularization, a cytokine, a growth factor, or ascorbic acid.

IC ICM A01N063-00  
 ICS A61F013-00; C12N005-00; A61K048-00

NCL 424093210

CC 63-7 (Pharmaceuticals)

IT Astrocyte

Chondrocyte

Epithelium

Fibroblast

Ganglion

Hematopoietic precursor cell

Human

Myoblast

Neuroglia

**Osteoblast**

Vaccines

(hybrid matrix implants and explants)

IT Angiogenic factors

Collagen fibers

Collagens, biological studies

Cytokines

Enzymes, biological studies

Fibrins

Gelatins, biological studies

Glass, biological studies

**Growth factors, animal**

Peptides, biological studies

**Platelet-derived growth factors**



Polyoxyalkylenes, biological studies  
 Polysulfones, biological studies  
 Proteoglycans, biological studies  
 RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hybrid matrix implants and explants)

IT **Prosthetic materials and Prosthetics**  
 (implants; hybrid matrix implants and explants)

IT **Transforming growth factors**  
 RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (.alpha.-; hybrid matrix implants and explants)

IT **Transforming growth factors**  
 RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (.beta.-; hybrid matrix implants and explants)

IT 50-81-7, Ascorbic acid, biological studies 9001-27-8, Factor VIII  
 9001-45-0, .beta.-Glucuronidase 9002-68-0, Fsh 9003-05-8,  
 Polyacrylamide 9003-53-6, Polystyrene 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9005-25-8,  
 Starch, biological studies 9005-32-7, Alginic acid 9005-35-0, Calcium alginate 9005-49-6, Heparin, biological studies 9007-12-9, Calcitonin 9025-35-8, .alpha.-Galactosidase 9025-60-9, Chondroitin 6-sulfatase 9031-11-2, .beta.-Galactosidase 9041-92-3, .alpha.1-Antitrypsin 9050-30-0, Heparan sulfate 9073-56-7, .alpha.-Iduronidase 9077-06-9, Heparan N-sulfatase 12629-01-5, Human growth hormone 24937-78-8, Eva 25249-16-5, Poly(2-hydroxyethyl methacrylate) 25322-68-3, Peg 26780-50-7, Glycolide-lactide copolymer 37228-64-1, .beta.-Glucosylceramidase 37288-40-7, .alpha.-N-Acetylglucosaminidase 57680-56-5, Sucrose octasulfate 60320-99-2, N-Acetylglucosamine 6-sulfatase 62229-50-9, Egf 72025-60-6, Leukotriene C4 79955-83-2, Acetyl CoA:.alpha.-Glucosaminide N-acetyltransferase 106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic fibroblast growth factor 106956-32-5, Oncostatin M 127464-60-2, Vascular endothelial growth factor 143011-72-7, G-CSF 188417-84-7, VEGF C 192662-83-2, Vascular endothelial growth factor B 193363-12-1, Vegf D  
 RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hybrid matrix implants and explants)

IT 9002-64-6, Parathyroid hormone 9004-10-8, Insulin, biological studies 9061-61-4, Nerve growth factor 11096-26-7, Erythropoietin 67763-96-6, Insulin like growth factor 1 169494-85-3, Leptin  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hybrid matrix implants and explants)

REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 6 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:502732 HCAPLUS

DOCUMENT NUMBER: 137:58022

TITLE: Cartilage alterations by administering to joints chondrocytes comprising a heterologous polynucleotide  
 INVENTOR(S): Glorioso, Joseph C.; Evans, Christopher H.; Robbins, Paul D.; Kane, Richard

PATENT ASSIGNEE(S): University of Pittsburgh of the Commonwealth System of Higher Education, USA

SOURCE: U.S., 55 pp., Cont.-in-part of U.S. 5,858,355.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 8  
 PATENT INFORMATION:

| PATENT NO.                                                                | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------------------------------------------------------------------|------|----------|-----------------|----------|
| US 6413511                                                                | B1   | 20020702 | US 1995-466932  | 19950606 |
| US 5858355                                                                | A    | 19990112 | US 1995-381603  | 19950127 |
| CA 2224176                                                                | AA   | 19961212 | CA 1996-2224176 | 19960605 |
| WO 9639196                                                                | A1   | 19961212 | WO 1996-US8899  | 19960605 |
| W: AU, CA, JP                                                             |      |          |                 |          |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE    |      |          |                 |          |
| AU 9661522                                                                | A1   | 19961224 | AU 1996-61522   | 19960605 |
| AU 720762                                                                 | B2   | 20000608 |                 |          |
| EP 828518                                                                 | A1   | 19980318 | EP 1996-919090  | 19960605 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI |      |          |                 |          |
| JP 2000500641                                                             | T2   | 20000125 | JP 1997-501361  | 19960605 |

PRIORITY APPLN. INFO.:

|                |    |          |
|----------------|----|----------|
| US 1990-630981 | B2 | 19901220 |
| US 1992-963928 | B1 | 19921020 |
| US 1993-27750  | B2 | 19930308 |
| US 1994-183563 | B2 | 19940118 |
| US 1995-381603 | A2 | 19950127 |
| US 1995-466932 | A  | 19950606 |
| WO 1996-US8899 | W  | 19960605 |

AB The invention concerns a method of introducing at least one DNA sequence expressing a protein or protein fragment which substantially alleviates articular cartilage defects. The protein fragment of polypeptide could be TGF- $\beta$ .1 or IRAP glycoprotein. This method involves in vitro culture of chondrocytes, transfection of the chondrocytes with a recombinant vector housing the DNA sequence to be expressed, and delivery of the transfected chondrocytes to the damaged cartilage region. This method can also be used in tandem with synovial cell delivery techniques of the invention. This method is also useful as a model in animal studies regarding joint pathologies.

IC A61K048-00; A01K067-00; A01N063-00; C12N015-00

NCL 424093200

CC 2-10 (Mammalian Hormones)  
 Section cross-reference(s): 3

IT **Bone morphogenetic proteins**  
 Interleukin 1 receptors  
 Interleukin 10  
 Interleukin 13  
 Interleukin 4  
 Polynucleotides  
 Tumor necrosis factor receptors  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (cartilage alterations by administering to joints chondrocytes comprising a heterologous polynucleotide)

IT **Transforming growth factors**  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (.alpha.-; cartilage alterations by administering to joints

chondrocytes comprising a heterologous polynucleotide)

IT **Transforming growth factors**  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (.beta.1-; cartilage alterations by administering to joints  
 chondrocytes comprising a heterologous polynucleotide)

IT **Transforming growth factors**  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (.beta.2-; cartilage alterations by administering to joints  
 chondrocytes comprising a heterologous polynucleotide)

IT **Transforming growth factors**  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (.beta.3-; cartilage alterations by administering to joints  
 chondrocytes comprising a heterologous polynucleotide)

IT **62031-54-3, Fibroblast growth factor 67763-96-6,**  
 Insulin-like growth factor I 124861-55-8, TIMP-2 140208-24-8, TIMP-1  
 145809-21-8, TIMP-3  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (cartilage alterations by administering to joints chondrocytes  
 comprising a heterologous polynucleotide)

IT 7757-93-9 9002-04-4, Thrombin **9004-54-0**, Dextran, biological  
 studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (cartilage alterations by administering to joints chondrocytes  
 comprising a heterologous polynucleotide)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 7 OF 43 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2002:482991 HCAPLUS  
 DOCUMENT NUMBER: 137:52468  
 TITLE: Crosslinkable macromers for preparation of matrixes  
 for implanted articles  
 INVENTOR(S): Chudzik, Stephen J.; Clapper, David L.  
 PATENT ASSIGNEE(S): Surmodics, Inc., USA  
 SOURCE: U.S., 14 pp., Cont.-in-part of U. S. 6,156,345.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 6410044    | B1   | 20020625 | US 2000-571525  | 20000516 |
| US 6007833    | A    | 19991228 | US 1998-121248  | 19980723 |
| US 6156345    | A    | 20001205 | US 1999-469976  | 19991221 |
| WO 2002100453 | A1   | 20021219 | WO 2001-US18345 | 20010607 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,  
 RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,  
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2003031697 A1 20030213 US 2002-176203 20020620

PRIORITY APPLN. INFO.:

US 1998-78607P P 19980319

US 1998-121248 A3 19980723

US 1999-469976 A2 19991221

US 2000-571525 A1 20000516

AB A crosslinkable macromer system and related methods of prep. the system and using the system in the form of a crosslinked matrix between a tissue site and an implant article, such as a tissue implant or on the porous surface of a prosthetic device, is described. The macromer system includes two or more polymer-pendent polymerizable groups and one or more initiator groups (e.g., polymer-pendent initiator groups). The polymerizable groups and the initiator group(s), when polymer-pendent, can be pendent on the same or different polymeric backbones. The macromer system provides advantages over the use of polymerizable macromers and sep., low mol. wt. initiators, including advantages with respect to such properties as nontoxicity, efficiency, and soly. A macromer system of the invention can be used as an interface between the tissue site and implant article in a manner sufficient to permit tissue growth through the crosslinked matrix and between the tissue site and implant. In a preferred embodiment, polymers with pendent polymerizable groups, for use in the macromer system, are prep. by reacting a polysaccharide polymer with a reactive moiety in an org., polar solvent, such as formamide. For example, a biodegradable tissue adhesive was prep. contg. (i) 5% polymerizable hyaluronic acid, prep. by reaction of hyaluronic acid and glycidyl acrylate in dry formamide, and (ii) 2% photoderivatized polyacrylamide, prep. from acrylamide and N-(3-aminopropyl)methacrylamide (APMA). The max. force generated by the adhesive prep. was 0.53 kg compared to 0.49 kg obtained for cyanoacrylate adhesive. Also, the photoderivatized polyacrylamide prep. was used in combination with polymerizable collagen (a reaction product of a mixt. of type I and type III collagen with acryloyl chloride) for prepn. of a scaffold contg. **bone** morphogenetic protein (BMP-7). The exptl. disks of solidified collagen scaffold contg. BMP-7 stimulated **bone** formation in a rat cranial onlay implant model.

IC ICM A61F002-06

ICS A61F002-28; A61F013-00; A61F047-30

NCL 424423000

CC 63-8 (Pharmaceuticals)

Section cross-reference(s): 35, 36

IT **Bone morphogenetic proteins**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(7; prepn. of crosslinkable macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)

IT **Prosthetic materials and Prosthetics**

(implants, vascular; prepn. of crosslinkable macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)

IT **Dental materials and appliances**

**Prosthetic materials and Prosthetics**

(implants; prepn. of crosslinkable macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)

IT Animal tissue

Antibacterial agents

Antimicrobial agents

**Bone formation**

Crosslinking

Immobilization, molecular

Polymerization catalysts

Transplant and Transplantation

Wound healing promoters

(prepn. of crosslinkable macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)

IT 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9005-25-8, Starch, biological studies 9005-49-6, Heparin, biological studies 9007-28-7, Chondroitin sulfate 9012-76-4, Chitosan 9042-14-2, Dextran sulfate 9050-30-0, Heparan sulfate 9056-36-4, Keratan sulfate 24967-94-0, Dermatan sulfate

RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(prepn. of crosslinkable macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 8 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:409132 HCAPLUS

DOCUMENT NUMBER: 136:391057

TITLE: Drug release from polymer matrixes through mechanical stimulation

INVENTOR(S): Lee, Kuen Yong; Mooney, David J.

PATENT ASSIGNEE(S): The Regents of the University of Michigan, USA

SOURCE: U.S. Pat. Appl. Publ., 11 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002064559 | A1   | 20020530 | US 2001-983320  | 20011024 |
| WO 2002078601 | A2   | 20021010 | WO 2001-US51603 | 20011026 |
| WO 2002078601 | C1   | 20021107 |                 |          |
| WO 2002078601 | A3   | 20030227 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-243813P P 20001027

AB A method for drug delivery and polymer matrix suited to the method are disclosed. The polymer matrix has reversibly bound thereto a drug or combination of drugs, and is capable of releasing the drug or combination of drugs in response to mech. stimulation of the polymer matrix. According to the method of this invention, such a polymer matrix is delivered to an in vivo locus, e.g., the site of a wound, trauma, etc., and mech. stimulation of said polymer matrix is effected in vivo, thereby releasing the drug or combination of drugs in the area of the in vivo

locus. Alginate hydrogels were prepd. comprising Protanal, Trypan blue as a model drug, and CaSO<sub>4</sub>. One group of the sample hydrogels were subjected to mech. stimulation comprising three cycles of compression/relaxation by using a mech. tester. Release of the trypan blue drug from the compressed hydrogels increased steadily over the course of compression/relaxation cycles.

IC ICM A61K031-727  
ICS A61K009-14  
NCL 424486000  
CC 63-6 (Pharmaceuticals)  
IT **Bone morphogenetic proteins**  
Collagens, biological studies  
Fibrins  
Gelatins, biological studies  
**Growth factors, animal**  
**Platelet-derived growth factors**  
Polymers, biological studies  
Proteins  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(drug release from polymer matrixes through mech. stimulation)  
IT **Transforming growth factors**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.-; drug release from polymer matrixes through mech. stimulation)  
IT **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic acid 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9005-35-0, Calcium alginate 9005-38-3D, Sodium alginate, heparin conjugates 9005-49-6D, Heparin, alginate conjugates 9012-36-6, Agarose 9019-41-4, Barium alginate 9057-02-7, Pullulan 9061-61-4, Nerve growth factor 37251-44-8, Magnesium alginate 54077-22-4, Strontium alginate 106096-93-9, Basic fibroblast growth factor 127464-60-2, Vascular endothelial growth factor  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(drug release from polymer matrixes through mech. stimulation)

L31 ANSWER 9 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:353301 HCAPLUS

DOCUMENT NUMBER: 136:359642

TITLE: Mineralized collagen-polysaccharide matrix for  
**bone** and cartilage repair

INVENTOR(S): Liu, Lin Shu; Spiro, Robert C.

PATENT ASSIGNEE(S): Orquest, Inc., USA

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND                                                                                                                                                                                                                                                                                                                                                                                       | DATE     | APPLICATION NO. | DATE     |
|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 2002036147 | A1                                                                                                                                                                                                                                                                                                                                                                                         | 20020510 | WO 2001-US42477 | 20011005 |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002011850 A5 20020515 AU 2002-11850 20011005

PRIORITY APPLN. INFO.:

US 2000-703438 A 20001031

WO 2001-US42477 W 20011005

- AB A matrix and a method for prepg. it are provided to support the growth of tissue, such as **bone**, cartilage or soft connective tissue. A polysaccharide is reacted with an oxidizing agent to open sugar rings on the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent linkages to mineralized collagen. The matrix can be implanted or injected, or the polyaldehyde polysaccharide and mineralized collagen starting minerals can be sep. injected to form the matrix in situ. Mineralized Type I collagen and polysaccharide-polyaldehyde were prepd. by mixing collagens with hyaluronate-polyaldehyde soln. Sodium cyanoborohydride was added to the mixt. to the final concn. of 10 mM. The resulting slurry was then poured into a mold and lyophilized. This formed a matrix, which was washed with water to remove NaCNBH3 and re-lyophilized. The surface property, structures and biol. activity of the matrixes were controlled by altering the ratio of the collagen to the polysaccharides, the type of polysaccharides, the d. of aldehyde groups generated on the polysaccharides, the d. of matrix, as well as the process of lyophilization.
- IC ICM A61K038-16  
 ICS A61K038-17; A61K009-14; A61K035-14
- CC 63-6 (Pharmaceuticals)
- ST mineralized collagen polysaccharide matrix **bone** cartilage repair
- IT **Growth factors, animal**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (ADMP 1; mineralized collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT **Prosthetic materials and Prosthetics**  
 (implants; mineralized collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT **Bone**  
 Cartilage  
 Drying  
 Freeze drying  
 (mineralized collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT **Bone morphogenetic proteins**  
 Fibrins  
**Growth factors, animal**  
 Interleukins  
**Platelet-derived growth factors**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (mineralized collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Polysaccharides, biological studies  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (oxidized, reaction products with collagens; mineralized collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Collagens, biological studies  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (reaction products with polysaccharides; mineralized

collagen-polysaccharide matrix for **bone** and cartilage repair)

IT Connective tissue  
(soft; mineralized collagen-polysaccharide matrix for **bone**  
and cartilage repair)

IT Drug delivery systems  
(sustained-release; mineralized collagen-polysaccharide matrix for  
**bone** and cartilage repair)

IT Collagens, biological studies  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)  
(type I, reaction products with polysaccharides; mineralized  
collagen-polysaccharide matrix for **bone** and cartilage repair)

IT Collagens, biological studies  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)  
(type II, reaction products with polysaccharides; mineralized  
collagen-polysaccharide matrix for **bone** and cartilage repair)

IT **Transforming growth factors**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.-; mineralized collagen-polysaccharide matrix for **bone**  
and cartilage repair)

IT **9004-54-ODP**, Dextran, reaction products with collagens  
9004-61-9DP, Hyaluronic acid, reaction products with collagens  
9005-32-7DP, Alginic acid, reaction products with collagens 9007-28-7DP,  
Chondroitin sulfate, reaction products with collagens 9042-14-2DP,  
Dextran sulfate, reaction products with collagens 9050-30-ODP, Heparan  
sulfate, reaction products with collagens 9056-36-4DP, Keratan sulfate,  
reaction products with collagens 24967-94-ODP, Dermatan sulfate,  
reaction products with collagens 70226-44-7DP, Heparan, reaction  
products with collagens  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)  
(mineralized collagen-polysaccharide matrix for **bone** and  
cartilage repair)

IT **61912-98-9**, Insulin-like growth factor **62031-54-3**,  
Fibroblast growth factor 62683-29-8, CSF  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(mineralized collagen-polysaccharide matrix for **bone** and  
cartilage repair)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 10 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:185399 HCAPLUS

DOCUMENT NUMBER: 136:229029

TITLE: Method for precipitating mono and multiple layers of  
organophosphoric and organophosphonic acids and the  
salts thereof in addition to use thereof

INVENTOR(S): Hofer, Rolf; Pawlak, Michael; Textor, Marcus;  
Schuermann-Mader, Eveline; Ehrat, Markus; Tosatti,  
Samuele

PATENT ASSIGNEE(S): Zeptosens A.-G., Switz.

SOURCE: PCT Int. Appl., 88 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1



## PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | KIND | DATE     | APPLICATION NO. | DATE       |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|------------|
| WO 2002020873                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | A2   | 20020314 | WO 2001-EP10077 | 20010831   |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,<br>HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,<br>LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,<br>RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,<br>VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,<br>DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,<br>BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG |      |          |                 |            |
| AU 2001089859                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | A5   | 20020322 | AU 2001-89859   | 20010831   |
| PRIORITY APPLN. INFO.:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |      |          | CH 2000-1732    | A 20000905 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |      |          | WO 2001-EP10077 | W 20010831 |

OTHER SOURCE(S): MARPAT 136:229029

AB The invention relates to a method for pptg. mono or multiple layers of organophosphosphoric acids of general formula (I(A)) Y-B-OPO<sub>3</sub> H<sub>2</sub> (IA) or organophosphonic acids of general formula (I(B)) Y-B-PO<sub>3</sub> H<sub>2</sub> (IB) and the salts thereof, wherein B is an alkyl, alkenyl, alkynyl, aryl, aralkyl, hetaryl or hetaryl alkyl radical and Y is hydrogen or a functional group from the hydroxy, carboxy, amino, optionally low-alkyl- substituted mono or dialkylamino series, thiol, or a neg. acid group from the ester, phosphate, phosphonate, sulfate, sulfonate, maleimide, succinimidyl, epoxy, acrylate series. A biol., biochem. or synthetic indicator element can be coupled to B or Y as addn. or substitution reaction, whereby compds. can also be added imparting on the substrate surface a resistance against protein absorption and/or cell adhesion and in the B chain can be, optionally, composed of one or more ethylene oxide groups rather than one or more CH<sub>2</sub> groups. According to the invention, said pptn. occurs on the surfaces of the substrates of pure or mixed oxides, nitrides or carbides of metals and semi-conductors. The invention is characterized in that the water-sol. salts composed of formula (IA) or (IB) are used to treat said surfaces, esp. the surfaces of sensor platforms, implants and medical accessory devices. The invention also relates to the use thereof as part of coated sensor platforms, implants and medical accessory devices in addn. to novel organophosphosphoric acids and organophosphonic acids themselves. The optionally substituted compds. of general formula (IA) and (IB), wherein the groups B and Y have the above mentioned designations i.e. optionally substituted alkyl, alkenyl, alkynyl, aryl, aralkyl, hetaryl or hetaryl, are equally called organophosphoric acids or phosphonic acids.

IC ICM C23C022-00

CC 9-1 (Biochemical Methods)

Section cross-reference(s): 14, 17, 29, 63, 64

IT **Dental materials and appliances**

(fillings; method for pptg. mono and multiple layers of organophosphoric and organophosphonic acids and the salts thereof in addn. to use thereof)

IT **Prosthetic materials and Prosthetics**

(implants, surfaces; method for pptg. mono and multiple layers of organophosphoric and organophosphonic acids and the salts thereof in addn. to use thereof)

IT Adhesion, biological

Adhesion, physical

Analysis  
Animal tissue  
Bioindicators (whole organism)  
Blood analysis  
Calibration  
Ceramics  
Chelating agents  
Combinatorial chemistry  
Contact resistance  
Culture media  
Desorption  
Detergents  
Diffraction gratings  
Egg yolk  
Endoscopes  
Fermentation  
Food analysis  
Hydrophilicity  
Hydrophobicity  
Immobilization  
Immunoassay  
Indicators  
Labels  
Lymph  
Microsome  
Monolayers  
Multilayers  
Optical fibers  
Optical transmission  
Pathogen  
Pathogenic bacteria  
Pharmaceutical analysis  
Prisms  
**Prosthetic materials and Prosthetics**  
Salmonella  
Semiconductor materials  
Separation  
Soil analysis  
Surface reaction  
Therapy  
Toxicology  
Urine analysis  
Veterinary medicine  
Virus

(method for pptg. mono and multiple layers of organophosphoric and organophosphonic acids and the salts thereof in addn. to use thereof)

IT

Antibodies

Antigens

**Bone morphogenetic proteins**

DNA

Glycoproteins

**Growth factors, animal**

Oligonucleotides

Peptides, analysis

RNA

Receptors

RL: ARU (Analytical role, unclassified); DEV (Device component use); PEP

(Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process); USES (Uses)  
(phosphoric and phosphonic acid derivs.; method for pptg. mono and multiple layers of organophosphoric and organophosphonic acids and the salts thereof in addn. to use thereof)

IT **Bone**

(prostheses; method for pptg. mono and multiple layers of organophosphoric and organophosphonic acids and the salts thereof in addn. to use thereof)

IT **Transforming growth factors**

RL: ARU (Analytical role, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process); USES (Uses)  
(.beta.-, phosphoric and phosphonic acid derivs.; method for pptg. mono and multiple layers of organophosphoric and organophosphonic acids and the salts thereof in addn. to use thereof)

IT 107-73-3, Phosphorylcholine **9004-54-0**, Dextran, biological studies 9005-49-6, Heparin, biological studies 9005-64-5, Tween 20 25322-68-3, Polyethylene glycol  
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); BIOL (Biological study); PROC (Process)

(method for pptg. mono and multiple layers of organophosphoric and organophosphonic acids and the salts thereof in addn. to use thereof)

L31 ANSWER 11 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:143320 HCAPLUS

DOCUMENT NUMBER: 136:189420

TITLE: Tissue engineering composite for purposes of repairing damaged tissues and reconstructing new tissues

INVENTOR(S): Burg, Karen J. L.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 10 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 2002022883 | A1   | 20020221 | US 2001-879360  | 20010612 |

PRIORITY APPLN. INFO.: US 2000-211147P P 20000613

AB The invention provides a biocompatible composite for use in a living subject for purposes of repairing damaged tissues and reconstructing a new tissue. The composite includes a biodegradable or absorbable three-dimensional support construct, a liq. or viscous fluid forming a gel matrix or viscous fluid when delivered to an area of interest in a living subject. The biodegradable construct provides an ideal surface for cell or cell ext. attachment, while the gel matrix or viscous fluid acts as both a carrier material and a separator for maintaining the space between the constructs as well as the structural integrity of the developing issue. Collagen beads were dynamically loaded for 48 h with rat aortic smooth muscle cells, then were mixed and gelled in alginates of 0.5, 1.0, and 2.0% gel strengths following cultivation. Composites were similarly prepd. and 1 mL of the composite was injected s.c. in each exptl. female Lewis rat. Samples were retrieved after 2, 4, and 6 wk and assessed

histol. using a series of cell-specific stains. The in vitro studies demonstrated that the 2.0 percent gel did not allow the high cell viabilities and the low gel strength of 0.5 percent did not maintain the necessary polymeric form. The in vivo work demonstrated that the material can be readily injected and thus is clin. feasible: All composites showed minimal inflammation and minimal fibrous encapsulation, and they appeared to be able to readily conform to irregular defects.

- IC ICM A61F002-08  
ICS A61F002-12; A61F002-10  
NCL 623008000  
CC 63-7 (Pharmaceuticals)  
IT **Prosthetic materials and Prosthetics**  
(composites; tissue engineering composite for purposes of repairing damaged tissues and reconstructing new tissues)  
IT **Bone**  
(demineralized; tissue engineering composite for purposes of repairing damaged tissues and reconstructing new tissues)  
IT **Prosthetic materials and Prosthetics**  
(implants; tissue engineering composite for purposes of repairing damaged tissues and reconstructing new tissues)  
IT **Growth factors, animal**  
Hormones, animal, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tissue engineering composite for purposes of repairing damaged tissues and reconstructing new tissues)  
IT 50-21-5D, Lactic acid, copolymer with lysine and RGD peptide 56-87-1D, Lysine, copolymer with lactic acid and RGD peptide 9000-07-1, Carrageenan 9002-89-5 9003-05-8 9003-11-6, Poly(ethylene oxide)-poly(propylene oxide) 9004-34-6, Cellulose, biological studies 9004-53-9, Dextrin **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic acid 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9007-28-7, Chondroitin sulfate 9012-36-6, Agarose 9012-76-4, Chitosan 24980-41-4, Polycaprolactone 25104-18-1, Polylysine 25248-42-4, Polycaprolactone 25322-68-3, Polyethylene glycol 26009-03-0, Polyglycolide 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26202-08-4, Polyglycolide 26680-10-4, Polylactide 31621-87-1, Polydioxanone 38000-06-5, Polylysine 156461-57-3, Lactic acid-Lysine copolymer  
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(tissue engineering composite for purposes of repairing damaged tissues and reconstructing new tissues)

L31 ANSWER 12 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:72718 HCAPLUS

DOCUMENT NUMBER: 136:123690

TITLE: Methods for stabilizing drugs encapsulated in biodegradable controlled-release polymers

INVENTOR(S): Schwendeman, Steven P.; Zhu, Gaozhong; Bentz, Hanne; Hubbell, Jeffrey A.; Jiang, Wenlei; Shenderova, Anna; Kang, Jichao

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 22 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE       |
|------------------------|------|----------|-----------------|------------|
| US 2002009493          | A1   | 20020124 | US 2000-738961  | 20001215   |
| PRIORITY APPLN. INFO.: |      |          | US 1999-170983P | P 19991215 |

AB Methods for reducing or inhibiting the irreversible inactivation of water-sol. drugs in biodegradable polymeric delivery systems which are designed to release such agents over a prolonged period of time, such as PLGA delivery systems are provided. The method comprises prepg. a PLGA delivery systems whose microclimate, i.e., the pores where the active agent resides, uniformly or homogeneously maintain a pH of between 3 and 9, preferably between 4 and 8, more preferably between 5 and 7.5 during biodegrdn. Depending on the size of the delivery system, and the initial bulk permeability of the polymer, this result is achieved by (a) incorporating a water-sol. carrier into the delivery system, (b) incorporating a select basic additive (or antacid) into the delivery system, (c) incorporating both a water sol. carrier and a select basic additive into the delivery system, (d) adding a pore forming mol. for increasing the rate of release of low mol. wt. monomers and oligomers into the delivery system, (e) using a PLGA polymer with reduced glycolide content, i.e. PLGA contg. 100 to 75% lactide and 0 to 25% glycolide (f) using a microencapsulation method that yields a more extensive pore-network, e.g., oil-in-oil emulsion-solvent extn. as opposed to water-in-oil-in water-solvent evapn. method, and (g) combinations thereof. Tissue plasminogen activator (tPA) was successfully encapsulated into PLGA implants. Controlled release systems for local delivery was developed by using hydrogel to control wound healing. A multi-drug controlled release implant with tPA encapsulated was also tested for the intraocular management of proliferative vitreoretinopathy. Here, 10% tPA powder was encapsulated as received (2% tPA, 75% arginine, 22% phosphoric acid, and 1% Polysorbate 80) with or without 3% Mg(OH)<sub>2</sub> into PLGA milli-cylinders. Arginine-HCl and BSA were added in the release medium to improve the stability of released tPA. With Mg(OH)<sub>2</sub> encapsulated, the 1-mo release of tPA was increased from 77.1 to 98.0% and the recovery (released part + active residue) was increased from 82.7 to 100.1%, resp.

IC ICM A61K009-14  
NCL 424486000  
CC 63-6 (Pharmaceuticals)  
IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(2; methods for stabilizing drugs encapsulated in biodegradable controlled-release polymers)

IT 546-93-0, Magnesium carbonate 1305-62-0, Calcium hydroxide, biological studies 1309-42-8, Magnesium hydroxide 1309-48-4, Magnesium oxide, biological studies 1339-92-0, Basic aluminum carbonate 3486-35-9, Zinc carbonate 7758-87-4, Calcium phosphate 7779-90-0, Zinc phosphate 9000-01-5, Gum arabic **9004-54-0**, Dextran, biological studies 10361-65-6, Ammonium phosphate 13682-92-3, Dihydroxyaluminum aminoacetate 14987-04-3, Magnesium trisilicate 16482-55-6, Dihydroxyaluminum sodium carbonate 20427-58-1, Zinc hydroxide 21645-51-2, Aluminum hydroxide, biological studies 74978-16-8, Magaldrate  
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods for stabilizing drugs encapsulated in biodegradable

controlled-release polymers)  
 IT 143-67-9, Vinblastine sulfate 2068-78-2, Vincristine sulfate  
 62031-54-3, Fibroblast growth factor 106096-93-9, Basic  
 Fibroblast growth factor 139639-23-9, Tissue plasminogen activator  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic  
 use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (methods for stabilizing drugs encapsulated in biodegradable  
 controlled-release polymers)

L31 ANSWER 13 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:906235 HCAPLUS

DOCUMENT NUMBER: 136:25166

TITLE: Method for composite cell-based implants using mineral  
 or polymeric microcarriers

INVENTOR(S): Frondoza, Carmelita G.; Hungerford, David S.; Shikani,  
 Alan H.; Domb, Abraham J.; Fink, David J.; Bloom,  
 Leonard

PATENT ASSIGNEE(S): Chondros, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U. S.  
 Ser. No. 825,632.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE        |
|------------------------|------|----------|-----------------|-------------|
| US 2001051834          | A1   | 20011213 | US 2001-922909  | 20010806    |
| US 2001014475          | A1   | 20010816 | US 2001-825632  | 20010404    |
| US 2002012705          | A1   | 20020131 | US 2001-929697  | 20010814    |
| US 6514522             | B2   | 20030204 |                 |             |
| US 2002123142          | A1   | 20020905 | US 2002-39718   | 20020103    |
| PRIORITY APPLN. INFO.: |      |          | US 1998-81016P  | P 19980408  |
|                        |      |          | US 1998-104842P | P 19981020  |
|                        |      |          | US 1999-275319  | A2 19990324 |
|                        |      |          | US 2000-712662  | A2 20001114 |
|                        |      |          | US 2001-825632  | A2 20010404 |
|                        |      |          | US 1999-165608P | P 19991115  |
|                        |      |          | US 2000-228855P | P 20000829  |

AB This invention is a method for the implantation of a combination of cells  
 or cell-microcarrier aggregates wherein one component comprises a solid  
 implantable construct and a second component comprises an injectable  
 formulation. For example, in one embodiment, the solid implant may be  
 first implanted to fill the majority of the cavity receiving the implant,  
 and then cells or cell-microcarrier aggregates in an injectable format,  
 with or without the addn. of gelling materials to promote rapid gelling in  
 situ, may be injected into spaces surrounding the solid implant in order  
 to secure the solid implant in the site and/or to promote rapid adherence  
 and/or integration of the solid implant to surrounding tissues. Also  
 contemplated in this embodiment is that the cellular compn. of the  
 injectable component may differ from that of the solid component. For  
 example, the solid implant may result from the culturing of chondrocytes  
 on microcarriers or scaffolds, e.g., calcium carbonate, calcium phosphate  
 or calcium sulfate, biopolymers, or synthetic polymers such as polylactic  
 acid, polyglycolic or their copolymers, thereby resulting in an implant  
 having cartilage-like properties, whereas the injectable cells or

aggregates may result from the culturing of stem cells, resulting thereby in cells capable of producing cells of a chondrogenic, fibroblastic, myoblastic or **osteoblastic** phenotype. In this example, cells in the injectable aggregates may promote the fixation to or rapid integration of the solid cartilage implant into surrounding cartilage, connective tissue, muscle or **bone**, resp. A method of treating a skin lesion or nose or ear defects comprises filling the lesion or defect with a solid cell-contg. implant along with an injectable cell-contg. formulation.

- IC ICM A61F002-02
- ICS A61F002-28
- NCL 623023720
- CC 63-7 (Pharmaceuticals)
- IT Animal tissue culture
  - Cell aggregation
  - Chondrocyte
  - Fibroblast
  - Gelation
  - Hydrogels
  - Myoblast
  - Osteoblast**
  - Polymerization
    - (composite of solid implant and injectable formulation of cells or cell-microcarrier aggregates for tissue repair)
- IT Antibodies
  - Bone morphogenetic proteins**
  - Cytokines
    - Growth factors, animal**
  - Integrins
  - Interleukins
  - Lymphotoxin
    - Platelet-derived growth factors**
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (fluid medium for injection contg.; composite of solid implant and injectable formulation of cells or cell-microcarrier aggregates for tissue repair)
- IT **Prosthetic materials and Prosthetics**
  - (implants; composite of solid implant and injectable formulation of cells or cell-microcarrier aggregates for tissue repair)
- IT **Bone**
  - Cartilage
    - (particles, microcarriers; composite of solid implant and injectable formulation of cells or cell-microcarrier aggregates for tissue repair)
- IT **Bone marrow**
  - (stroma, stem cells derived from; composite of solid implant and injectable formulation of cells or cell-microcarrier aggregates for tissue repair)
- IT Joint, anatomical
  - (temporal-**mandibular** or intervertebral, fibroblasts; composite of solid implant and injectable formulation of cells or cell-microcarrier aggregates for tissue repair)
- IT **62031-54-3, Fibroblast growth factor**
  - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
    - (fluid medium for injection contg.; composite of solid implant and injectable formulation of cells or cell-microcarrier aggregates for tissue repair)
- IT 471-34-1, Calcium carbonate, biological studies    1398-61-4, Chitin

7778-18-9, Calcium sulfate 9002-89-5, Polyvinyl alcohol 9002-98-6  
 9003-01-4, Poly(acrylic acid) 9004-54-0, Dextran, biological  
 studies 9004-61-9, Hyaluronic acid 9005-35-0, Calcium alginate  
 9012-36-6, Agarose 9012-76-4, Chitosan 10103-46-5, Calcium phosphate  
 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 25322-68-3,  
 Polyethylene glycol 26009-03-0, Polyglycolic acid 26023-30-3,  
 Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid  
 26124-68-5, Polyglycolic acid 34346-01-5, Glycolic acid-lactic acid  
 copolymer

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (microcarriers or scaffolds; composite of solid implant and injectable  
 formulation of cells or cell-microcarrier aggregates for tissue repair)

L31 ANSWER 14 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:850951 HCAPLUS

DOCUMENT NUMBER: 136:11086

TITLE: Methods and compositions for promoting angiogenesis  
 using monocytes

INVENTOR(S): Pawliuk, Robert; Leboulch, Philippe

PATENT ASSIGNEE(S): Genetix Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND                                                                                                                                                                                                                                                                                                                                                                                   | DATE     | APPLICATION NO. | DATE     |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 2001087314 | A1                                                                                                                                                                                                                                                                                                                                                                                     | 20011122 | WO 2001-US16026 | 20010518 |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG                                                                                                                                                                                                 |          |                 |          |
| US 2002034501 | A1                                                                                                                                                                                                                                                                                                                                                                                     | 20020321 | US 2001-860657  | 20010518 |

PRIORITY APPLN. INFO.: US 2000-205063P P 20000518

AB Novel compns. and methods for treating myocardial and peripheral ischemia are disclosed which employ monocytes to provide localized, controlled doses of secreted therapeutic proteins to selected tissue areas. These proteins can be naturally produced by monocytes, or produced following genetic transduction of monocytes or their progenitor cells with appropriate expression vectors.

IC ICM A61K035-14

ICS A61K038-19; A61P009-10

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 3, 15

IT **Bone morphogenetic proteins**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(2; methods and compns. for promoting angiogenesis using monocytes)

IT **Bone morphogenetic proteins**



RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(4; methods and compns. for promoting angiogenesis using monocytes)

IT **Bone morphogenetic proteins**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(7; methods and compns. for promoting angiogenesis using monocytes)

IT **Platelet-derived growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(B; methods and compns. for promoting angiogenesis using monocytes)

IT Macrophage inflammatory protein 1.alpha.

Macrophage inflammatory protein 1.beta.

Monocyte chemoattractant protein-1

**Osteopontin**

RANTES (chemokine)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods and compns. for promoting angiogenesis using monocytes)

IT Blood

**Bone marrow**

(monocyte purifn. from; methods and compns. for promoting angiogenesis using monocytes)

IT **Transforming growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.-; methods and compns. for promoting angiogenesis using monocytes)

IT 11096-26-7, Erythropoietin 65154-06-5, Paf **67763-96-6**, Igf-1  
106096-93-9, Basic fibroblast growth factor 114949-22-3, Activin  
123626-67-5, Endothelin-1 127464-60-2, Vascular endothelial growth  
factor A 186270-49-5, Angiopoietin 1 188417-84-7, Vascular endothelial  
growth factor C 192662-83-2, Vascular endothelial growth factor B  
193363-12-1, Vascular endothelial growth factor D 194368-66-6,  
Angiopoietin 2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods and compns. for promoting angiogenesis using monocytes)

IT **9015-73-0**

RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(methods and compns. for promoting angiogenesis using monocytes)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 15 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:792224 HCAPLUS

DOCUMENT NUMBER: 135:335182

TITLE: Collagen-polysaccharide matrix for treatment of  
**bone tumors**

INVENTOR(S): Heidaran, Mohammad; Spiro, Robert C.  
 PATENT ASSIGNEE(S): Orquest, Inc., USA  
 SOURCE: U.S., 9 pp., Cont.-in-part of U.S. 5,972,385.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|------------|------|----------|-----------------|----------|
| US 6309670 | B1   | 20011030 | US 1999-324792  | 19990603 |
| US 5866165 | A    | 19990202 | US 1997-783650  | 19970115 |
| US 5972385 | A    | 19991026 | US 1998-7731    | 19980115 |

PRIORITY APPLN. INFO.:  
 US 1997-783650 A2 19970115  
 US 1998-7731 A2 19980115

AB A method of treatment for **bone** tumors comprising administering a matrix comprising collagen, a polysaccharide and a differentiation factor is provided. A polysaccharide is reacted with an oxidizing agent to open sugar rings on the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent linkages to collagen. For example, the collagen/hyaluronic acid/TGF-.beta. combination inhibited growth of the **osteosarcoma** cell line SK-ES-1 more potently than a combination of TGF-.beta. and collagen in a monolayer culture.

IC ICM A61K009-10  
 ICS A61K047-42; A61K047-36

NCL 424486000

CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 2

ST collagen polysaccharide matrix differentiation factor antitumor **bone**

IT Antitumor agents  
 (Ewing's sarcoma; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)

IT Antitumor agents  
 (**bone**, metastasis; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)

IT Antitumor agents  
 (**bone**; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)

IT Antitumor agents  
 (carcinoma, **bone**; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)

IT Drug delivery systems  
 Oxidizing agents  
 (collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)

IT **Bone morphogenetic proteins**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)

IT Collagens, biological studies  
 Polysaccharides, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (collagen-polysaccharide matrix contg. differentiation factors for

- treatment of **bone** tumors)
- IT **Bone**, neoplasm  
(inhibitors; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT **Bone**, neoplasm  
(metastasis, inhibitors; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT Nervous system  
(neuroectoderm, neoplasm, inhibitors; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT Antitumor agents  
(neuroectoderm; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT **Bone**, neoplasm  
(**osteosarcoma**, inhibitors; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT Antitumor agents  
(**osteosarcoma**; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT Freeze drying  
(prepn. of collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT Antitumor agents  
(sarcoma; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT Cell differentiation  
(stimulation of; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT Drug interactions  
(synergistic; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT Collagens, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(type I; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT **Transforming growth factors**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.-; collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT 7790-28-5, Sodium periodate  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)
- IT **9004-54-0**, Dextran, biological studies    **9004-61-9**, Hyaluronic acid    **9005-32-7**, Alginic acid    **9007-28-7**, Chondroitin sulfate  
**9042-14-2**, Dextran sulfate    **9050-30-0**, Heparan sulfate    **9056-36-4**, Keratan sulfate    **24967-94-0**, Dermatan sulfate    **70226-44-7**, Heparan  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(collagen-polysaccharide matrix contg. differentiation factors for treatment of **bone** tumors)

REFERENCE COUNT: 14    THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 16 OF 43 HCAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2001:780648 HCAPLUS

DOCUMENT NUMBER: 135:335147  
 TITLE: Polymer-based injectable sustained release pharmaceutical compositions for peptide and protein drugs  
 INVENTOR(S): Lee; Hee-yong; Lee, Hye-suk; Kim, Jung-soo; Kim, Sang-beom; Lee, Ji-suk; Choi, Ho-il; Chang, Seung-gu  
 PATENT ASSIGNEE(S): Pepton Inc., S. Korea  
 SOURCE: PCT Int. Appl., 37 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.             | KIND                                                                                                                                                                                                                                                                                                                                                                       | DATE     | APPLICATION NO. | DATE       |
|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|------------|
| WO 2001078687          | A1                                                                                                                                                                                                                                                                                                                                                                         | 20011025 | WO 2001-KR462   | 20010322   |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |            |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG                                                                                                                                                                                     |          |                 |            |
| EP 1187602             | A1                                                                                                                                                                                                                                                                                                                                                                         | 20020320 | EP 2001-917893  | 20010322   |
| R:                     | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO                                                                                                                                                                                                                                                                                     |          |                 |            |
| US 2003026844          | A1                                                                                                                                                                                                                                                                                                                                                                         | 20030206 | US 2002-18870   | 20020418   |
| PRIORITY APPLN. INFO.: |                                                                                                                                                                                                                                                                                                                                                                            |          | KR 2000-20484   | A 20000418 |
|                        |                                                                                                                                                                                                                                                                                                                                                                            |          | KR 2000-49344   | A 20000824 |
|                        |                                                                                                                                                                                                                                                                                                                                                                            |          | WO 2001-KR462   | W 20010322 |

AB Controlled and sustained release injectable pharmaceutical compns. for a biopharmaceutical, such as peptides and proteins are described. Processes for prepn. of an injectable sustained release compn. comprises (i) a step of prepg. biodegradable porous microspheres having accessible ionic functional groups, (ii) a step of encapsulating a biopharmaceutical into the microspheres through ionic interaction by suspending or equilibrating the microspheres in a soln. contg. the biopharmaceutical, and (iii) a step of recovering and freeze-drying the biopharmaceutical-incorporated microspheres. For example, microspheres were prepd. by water/oil/water double emulsion solvent evapn. method using a hydrophilic 50:50 PLGA polymer (RG 502H), which contains free carboxy end groups. Deionized water (800 mL) was added to 1 g of PLGA polymer dissolved in 2 mL of methylene chloride and emulsified by sonication for 30 s using a probe type ultrasonic generator. This primary emulsion was dispersed into 200 mL of deionized water contg. 0.5% polyvinyl alc. (wt./vol.) in a vessel which connected to a const. temp. controller and mixed well by stirring for 15 min at 2500 rpm, 25.degree. using a mixer. After mixing for another 15 min at 1500 rpm, 25.degree., temp. of continuous phase was increased to 40.degree. to evap. methylene chloride. After 1 h stirring at 40.degree., 1500 rpm, temp. was decreased to 25.degree.. The hardened microspheres were collected by centrifugation and washed twice with 200 mL of deionized water, and then freeze-dried. The microspheres obtained were used for incorporation of protein drugs, i.e., ovalbumin, bovine serum albumin, human growth hormone, RNase A, or lysozyme through ionic

interaction by simply soaking and equilibrating the microspheres into a buffer soln. having an appropriate concn. of protein.

IC ICM A61K009-22

CC 63-6 (Pharmaceuticals)

IT **Growth factors, animal**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cartilage-inducing factor; prepn. of polymer-based injectable  
sustained-release microspheres for peptide and protein drugs)

IT **Growth factors, animal**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**osteogenic** growth factors; prepn. of polymer-based  
injectable sustained-release microspheres for peptide and protein  
drugs)

IT Annexins

**Bone morphogenetic proteins**

Caseins, biological studies

Collagens, biological studies

Fibrinogens

Hemoglobins

Interferons

Interleukin 1

Interleukins

Lymphotoxin

Ovalbumin

**Platelet-derived growth factors**

Polyanhydrides

Polycarbonates, biological studies

Polymer blends

Polysaccharides, biological studies

Proteins, general, biological studies

Transferrins

**Transforming growth factors**

Tumor necrosis factors

Zeins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of polymer-based injectable sustained-release microspheres for  
peptide and protein drugs)

IT 121-54-0, Benzethonium chloride 151-21-3, Sodium lauryl sulfate,  
biological studies 577-11-7, Docusate sodium 1393-25-5, Secretin  
1398-61-4, Chitin 1402-38-6, Oncostatin 8044-71-1, Cetrимide  
9001-25-6, Blood-coagulation factor VII 9001-28-9, Factor IX  
9001-63-2, Lysozyme 9002-01-1, Streptokinase 9002-60-2,  
Adrenocorticotrophic hormone, biological studies 9002-61-3, Human  
chorionic gonadotropin 9002-67-9, Luteinizing hormone 9002-68-0,  
Follicle stimulating hormone 9002-69-1, Relaxin 9002-71-5, Thyroid  
stimulating hormone 9002-72-6, Growth hormone 9002-89-5, Polyvinyl  
alcohol 9004-10-8, Insulin, biological studies 9004-53-9, Dextrin  
**9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic  
acid 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid  
9005-49-6, Heparin, biological studies 9007-12-9, Calcitonin  
9007-27-6, Chondroitin 9007-92-5, Glucagon, biological studies  
9011-97-6, Cholecystokinin 9012-76-4, Chitosan 9015-71-8,  
Corticotropin releasing factor 9034-39-3, Growth hormone releasing  
factor 9035-68-1, Proinsulin 9039-53-6, Urokinase 9041-92-3,  
.alpha.1-Antitrypsin 9054-89-1, Superoxide dismutase 9056-36-4,  
Keratan sulfate 9061-61-4, Nerve growth factor 11096-26-7,  
Erythropoietin 15802-18-3D, Cyanoacrylic acid, esters, polymers

24980-41-4, Polycaprolactone 25104-18-1, Poly(L-lysine) 25248-42-4, Polycaprolactone 25868-59-1 25931-47-9 26009-03-0, Polyglycolide 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26202-08-4, Polyglycolide 26680-10-4, Polylactide 26780-50-7, Poly(lactide-co-glycolide) 31621-87-1, Polydioxanone 34346-01-5, Resomer RG 502H 37221-79-7, Vasoactive intestinal polypeptide 38000-06-5, Poly(L-lysine) 52906-92-0, Motilin 57285-09-3, Inhibin 59392-49-3, Gastric inhibitory peptide 59763-91-6, Pancreatic polypeptide **61912-98-9**, Insulin-like growth factor **62229-50-9**, Epidermal growth factor 62683-29-8, Colony stimulating factor **67763-96-6**, Somatomedin C 77272-10-7, Macro cortin 80043-53-4, Gastrin releasing peptide 82657-92-9, Prourokinase 83652-28-2, Calcitonin gene-related peptide 85637-73-6, Atrial natriuretic factor 113189-02-9, Antihemophilic factor 139639-23-9, Tissue plasminogen activator

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 17 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:757812 HCAPLUS

DOCUMENT NUMBER: 135:308889

TITLE: Crosslinked polysaccharide drug carrier

INVENTOR(S): Spiro, Robert C.; Thompson, Andrea Y.; Liu, Linshu

PATENT ASSIGNEE(S): Orquest, Inc., USA

SOURCE: U.S., 7 pp., Cont.-in-part of U.S. Ser. No. 887,994, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE        |
|------------------------|------|----------|-----------------|-------------|
| US 6303585             | B1   | 20011016 | US 1998-110381  | 19980701    |
| US 2003012765          | A1   | 20030116 | US 2001-954855  | 20010917    |
| PRIORITY APPLN. INFO.: |      |          | US 1997-887994  | B2 19970703 |
|                        |      |          | US 1998-110381  | A1 19980701 |

AB A carrier and a method for prepg. it are provided for use in the delivery of therapeutic agents. A polysaccharide is reacted with an oxidizing agent to open sugar rings on the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent oxime linkages with a second polysaccharide and each of the first and second polysaccharide is selected from the group consisting of hyaluronic acid, dextran, dextran sulfate, chondroitin sulfate, dermatan sulfate, keratan sulfate, heparan, heparan sulfate and alginate. A hyaluronate amine deriv. was prepd. by treating hyaluronic acid with EDC and ethylenediamine.

IC ICM C08B037-00

ICS A61K031-715

NCL 514054000

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 33

IT **Bone formation**

Crosslinking

Dissolution rate

(crosslinked polysaccharide drug carrier)

IT **Growth factors, animal**

Polysaccharides, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(crosslinked polysaccharide drug carrier)

IT **9004-54-0**, Dextran, biological studies 9005-32-7, Alginic acid  
 9005-49-6, Heparin, biological studies 9007-28-7, Chondroitin sulfate  
 9042-14-2, Dextran sulfate 9050-30-0, Heparan sulfate 9056-36-4,  
 Keratan sulfate 24967-94-0, Dermatan sulfate  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (crosslinked polysaccharide drug carrier)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 18 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:661596 HCAPLUS

DOCUMENT NUMBER: 135:237110

TITLE: Cloning and characterization of chordin-like-2 protein  
 genes from human and mouse, diagnostic and therapeutic  
 use thereof

INVENTOR(S): Zhang, Ke; Linh, Cam; Nakayama, Naoki

PATENT ASSIGNEE(S): Amgen, Inc., USA

SOURCE: PCT Int. Appl., 167 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND                                                                                                                                                                                                                                                                                                                                           | DATE     | APPLICATION NO. | DATE     |
|---------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 2001064885 | A1                                                                                                                                                                                                                                                                                                                                             | 20010907 | WO 2001-US6891  | 20010302 |
| W:            | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG                                                                                                                                                         |          |                 |          |
| EP 1266000    | A1                                                                                                                                                                                                                                                                                                                                             | 20021218 | EP 2001-913290  | 20010302 |
| R:            | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR                                                                                                                                                                                                                                         |          |                 |          |

PRIORITY APPLN. INFO.: US 2000-186462P P 20000302  
 WO 2001-US6891 W 20010302

AB The invention provides protein and cDNA sequences for novel human and mouse chordin-like-2 protein CHL2, which has sequence similarity to chordin known as the **bone** morphogenetic protein (BMP) inhibitor. The invention also provides selective binding agents, vectors, host cells, and methods for producing CHL2 polyproteins. The tissue distribution pattern of the mRNA shows that CHL2 is involved in mouse articular chondrocytes, sternum, placenta, uterus, colon, and small intestine. CHL2 directly interacts with BMPs, and its inhibitory activity is demonstrated in CHL2 gene transfected cells, Xenopus embryo, and in transgenic mice. The murine CHL2 gene is mapped to chromosome 7 centromere. The invention further provides pharmaceutical compns. and methods for the diagnosis,

treatment, amelioration, and/or prevention of diseases, disorders, and conditions assocd. with CHL2 polyproteins.

- IC ICM C12N015-12  
ICS C07K014-47; C07K014-705; C12N015-62; C07K016-18; C07K016-28;  
G01N033-53; A61K038-17; C12Q001-68
- CC 2-10 (Mammalian Hormones)  
Section cross-reference(s): 1, 3, 63
- ST chordin like 2 protein CHL2 cDNA sequence human mouse; **bone**  
morphogenetic protein inhibition CHL2 gene diagnosis therapy
- IT **Bone morphogenetic proteins**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(2, inhibition by chordin-like-2 protein; cloning and characterization  
of chordin-like-2 protein genes from human and mouse, diagnostic and  
therapeutic use thereof)
- IT **Bone morphogenetic proteins**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(4, inhibition by chordin-like-2 protein; cloning and characterization  
of chordin-like-2 protein genes from human and mouse, diagnostic and  
therapeutic use thereof)
- IT **Bone morphogenetic proteins**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(5, inhibition by chordin-like-2 protein; cloning and characterization  
of chordin-like-2 protein genes from human and mouse, diagnostic and  
therapeutic use thereof)
- IT **Bone morphogenetic proteins**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(6, 14, inhibition by chordin-like-2 protein; cloning and  
characterization of chordin-like-2 protein genes from human and mouse,  
diagnostic and therapeutic use thereof)
- IT **Bone morphogenetic proteins**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(6, inhibition by chordin-like-2 protein; cloning and characterization  
of chordin-like-2 protein genes from human and mouse, diagnostic and  
therapeutic use thereof)
- IT **Growth factors, animal**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(chordin; cloning and characterization of chordin-like-2 protein genes  
from human and mouse, diagnostic and therapeutic use thereof)
- IT **Bone**  
(sternum, CHL2 mRNA expression in; cloning and characterization of  
chordin-like-2 protein genes from human and mouse, diagnostic and  
therapeutic use thereof)
- IT 57-55-6D, Propylene glycol, conjugates with chordin-like-2 protein  
9002-89-5D, Polyvinyl alcohol, conjugates with chordin-like-2 protein  
9003-11-6D, Ethylene oxide propylene oxide copolymer, conjugates with  
chordin-like-2 protein 9004-34-6D, Cellulose, conjugates with  
chordin-like-2 protein, biological studies **9004-54-0D**, Dextran,  
conjugates with chordin-like-2 protein, biological studies 9004-74-4D,  
Monomethoxy polyethylene glycol, conjugates with chordin-like-2 protein  
9065-38-7D, conjugates with chordin-like-2 protein 25322-68-3D,  
Polyethylene glycol, conjugates with chordin-like-2 protein  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cloning and characterization of chordin-like-2 protein genes from  
human and mouse, diagnostic and therapeutic use thereof)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



L31 ANSWER 19 OF 43 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2001:618469 HCAPLUS  
 DOCUMENT NUMBER: 135:170821  
 TITLE: **Osteogenic** devices and methods of use  
 thereof for repair of endochondral **bone** and  
**osteochondral** and chondral defects  
 INVENTOR(S): Rueger, David C.; Tucker, Marjorie A.; Chang, An-Cheng  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S. Pat. Appl. Publ., 59 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.             | KIND                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | DATE     | APPLICATION NO. | DATE     |
|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| US 2001016646          | A1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 20010823 | US 1998-45331   | 19980320 |
| PRIORITY APPLN. INFO.: |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          | US 1998-45331   | 19980320 |
| AB                     | Disclosed herein are improved <b>osteogenic</b> devices and methods of use thereof for repair of <b>bone</b> and cartilage defects. The devices and methods promote accelerated formation of repair tissue with enhanced stability using less <b>osteogenic</b> protein than devices in the art. Defects susceptible to repair with the instant invention include, but are not limited to: crit. size defects, non-crit. size defects, non-union fractures, fractures, <b>osteochondral</b> defects, subchondral defects, and defects resulting from degenerative diseases such as <b>osteochondritis</b> dissecans. |          |                 |          |
| IC                     | ICM C07K001-00<br>ICS C07K014-00; C07K017-00; A01N025-34; G01N033-53                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |          |                 |          |
| NCL                    | 530840000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |          |                 |          |
| CC                     | 63-7 (Pharmaceuticals)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |          |                 |          |
| ST                     | <b>osteogenic</b> device endochondral <b>bone</b> defect repair                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          |                 |          |
| IT                     | <b>Bone morphogenetic proteins</b><br>RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)<br>(10; <b>osteogenic</b> devices for repair of endochondral <b>bone</b> and <b>osteochondral</b> and chondral defects)                                                                                                                                                                                                                          |          |                 |          |
| IT                     | <b>Bone morphogenetic proteins</b><br>RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)<br>(11; <b>osteogenic</b> devices for repair of endochondral <b>bone</b> and <b>osteochondral</b> and chondral defects)                                                                                                                                                                                                                          |          |                 |          |
| IT                     | <b>Bone morphogenetic proteins</b><br>RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)<br>(12; <b>osteogenic</b> devices for repair of endochondral <b>bone</b> and <b>osteochondral</b> and chondral defects)                                                                                                                                                                                                                          |          |                 |          |
| IT                     | <b>Bone morphogenetic proteins</b><br>RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)<br>(15; <b>osteogenic</b> devices for repair of endochondral <b>bone</b> and <b>osteochondral</b> and chondral defects)                                                                                                                                                                                                                          |          |                 |          |

- IT **Bone morphogenetic proteins**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (16; **osteogenic** devices for repair of endochondral bone and **osteochondral** and chondral defects)
- IT **Bone morphogenetic proteins**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (3; **osteogenic** devices for repair of endochondral bone and **osteochondral** and chondral defects)
- IT **Bone morphogenetic proteins**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (4; **osteogenic** devices for repair of endochondral bone and **osteochondral** and chondral defects)
- IT **Bone morphogenetic proteins**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (5; **osteogenic** devices for repair of endochondral bone and **osteochondral** and chondral defects)
- IT Proteins, specific or class  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (60A; **osteogenic** devices for repair of endochondral bone and **osteochondral** and chondral defects)
- IT **Bone morphogenetic proteins**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (6; **osteogenic** devices for repair of endochondral bone and **osteochondral** and chondral defects)
- IT **Bone morphogenetic proteins**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (7; **osteogenic** devices for repair of endochondral bone and **osteochondral** and chondral defects)
- IT **Bone morphogenetic proteins**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (9; **osteogenic** devices for repair of endochondral bone and **osteochondral** and chondral defects)
- IT Proteins, specific or class  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (DPP; **osteogenic** devices for repair of endochondral bone and **osteochondral** and chondral defects)
- IT Proteins, specific or class  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF10; **osteogenic** devices for repair of endochondral  
**bone and osteochondral** and chondral defects)

IT Proteins, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF11; **osteogenic** devices for repair of endochondral  
**bone and osteochondral** and chondral defects)

IT Proteins, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF1; **osteogenic** devices for repair of endochondral  
**bone and osteochondral** and chondral defects)

IT Proteins, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF3; **osteogenic** devices for repair of endochondral  
**bone and osteochondral** and chondral defects)

IT Proteins, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF5; **osteogenic** devices for repair of endochondral  
**bone and osteochondral** and chondral defects)

IT Proteins, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF6; **osteogenic** devices for repair of endochondral  
**bone and osteochondral** and chondral defects)

IT Proteins, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF7; **osteogenic** devices for repair of endochondral  
**bone and osteochondral** and chondral defects)

IT Proteins, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF8; **osteogenic** devices for repair of endochondral  
**bone and osteochondral** and chondral defects)

IT Proteins, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF9; **osteogenic** devices for repair of endochondral  
**bone and osteochondral** and chondral defects)

IT Proteins, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(Vgl; **osteogenic** devices for repair of endochondral  
**bone and osteochondral** and chondral defects)

- IT Proteins, specific or class  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (Vgr; **osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT Cartilage  
 (articular; **osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT Drug delivery systems  
 (carriers; **osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT Medical goods  
 (containers; **osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT **Bone**  
 (demineralized; **osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT Cartilage  
 (formation; **osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT **Bone, disease**  
 (fracture; **osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT Containers  
 (medical; **osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT **Bone, disease**  
 Cartilage  
 (**osteochondritis** dissecans; **osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT Binders  
**Bone formation**  
 Protein sequences  
 Wetting agents  
 cDNA sequences  
 (**osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT Fibrins  
 Petrolatum  
 RL: DEV (Device component use); MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (**osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT Apatite-group minerals  
 Collagens, biological studies  
 RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (**osteogenic** devices for repair of endochondral **bone** and **osteochondral** and chondral defects)
- IT Fibrinogens  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (**osteogenic** devices for repair of endochondral **bone**

and **osteocondral** and chondral defects)

IT **Growth factors, animal**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(**osteogenic** protein 2; **osteogenic** devices for repair of endochondral **bone** and **osteocondral** and chondral defects)

IT **Growth factors, animal**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(**osteogenic** protein 3; **osteogenic** devices for repair of endochondral **bone** and **osteocondral** and chondral defects)

IT Fats and Glyceridic oils, biological studies

RL: DEV (Device component use); MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(sesame; **osteogenic** devices for repair of endochondral **bone** and **osteocondral** and chondral defects)

IT 69-65-8, mannitol 9004-32-4, carboxymethylcellulose 9004-34-6D, cellulose, alkyl derivs., biological studies **9004-54-0**, dextran, biological studies 9004-62-0, Hydroxyethylcellulose 9004-65-3, hydroxypropylmethylcellulose 9004-67-5, methylcellulose 9032-42-2, methylhydroxyethylcellulose

RL: DEV (Device component use); MOA (Modifier or additive use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(**osteogenic** devices for repair of endochondral **bone** and **osteocondral** and chondral defects)

IT 1306-06-5, hydroxyapatite 7758-87-4, tricalcium phosphate

RL: DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(**osteogenic** devices for repair of endochondral **bone** and **osteocondral** and chondral defects)

IT 9002-04-4, thrombin

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(**osteogenic** devices for repair of endochondral **bone** and **osteocondral** and chondral defects)

L31 ANSWER 20 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:581931 HCAPLUS

DOCUMENT NUMBER: 135:157661

TITLE: Extraction of growth factors from tissue

INVENTOR(S): Donda, Russell S.; Wironen, John F.; Seid, Christopher

PATENT ASSIGNEE(S): Regeneration Technologies, Inc., USA

SOURCE: PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

-----  
 WO 2001057082      A2      20010809      WO 2001-US3474      20010202  
 WO 2001057082      A3      20020221

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,  
 CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,  
 IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,  
 MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,  
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,  
 BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001041792      A1      20011115      US 2001-776619      20010202

PRIORITY APPLN. INFO.:      US 2000-180067P      P      20000203  
                                          US 2000-200842P      P      20000501  
                                          US 2000-215912P      P      20000703

AB    Disclosed are novel methods of obtaining **osteogenic** and other  
 growth factor compns. from alternative nonbone sources such as tissue or  
**bone** marrow, and methods of using the same. Also disclosed are  
 implants infused with growth factors obtained from the methods. An  
 example is given of extn. of growth factors from platelets.

IC    ICM C07K014-475

CC    63-3 (Pharmaceuticals)  
 Section cross-reference(s): 2

IT    **Prosthetic materials and Prosthetics**  
 (bioactive glass; extn. of growth factors from tissue)

IT    **Prosthetic materials and Prosthetics**  
 (ceramics; extn. of growth factors from tissue)

IT    Adipose tissue  
 Animal tissue  
       **Bone**  
       **Bone** marrow  
       Cadaver  
       Cartilage  
       Connective tissue  
       Muscle  
       Platelet (blood)  
       Skin  
       Solubilizers  
       (extn. of growth factors from tissue)

IT    **Platelet-derived growth factors**  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP  
 (Physical, engineering or chemical process); PUR (Purification or  
 recovery); THU (Therapeutic use); BIOL (Biological study); OCCU  
 (Occurrence); PREP (Preparation); PROC (Process); USES (Uses)  
 (extn. of growth factors from tissue)

IT    **Growth factors, animal**  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PUR  
 (Purification or recovery); THU (Therapeutic use); BIOL (Biological  
 study); OCCU (Occurrence); PREP (Preparation); USES (Uses)  
 (extn. of growth factors from tissue)

IT    **Prosthetic materials and Prosthetics**  
 (implants; extn. of growth factors from tissue)

IT    Angiogenic factors  
       **Bone morphogenetic proteins**  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP  
 (Physical, engineering or chemical process); PUR (Purification or

recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); USES (Uses) (platelet-derived; extn. of growth factors from tissue)

IT 50-01-1, Guanidine hydrochloride 56-81-5, Glycerol, processes 57-13-6, Urea, processes 151-21-3, Sodium dodecyl sulfate, processes 9002-93-1, Triton x100 9004-34-6, Cellulose, processes 9004-54-0, Dextran, processes 9004-61-9, Hyaluronic acid 9005-80-5, Inulin 9012-36-6, Agarose 9037-22-3, Amylopectin 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 26009-03-0, Polyglycolic acid 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 106392-12-5, pluronic F127  
RL: PEP (Physical, engineering or chemical process); PROC (Process) (extn. of growth factors from tissue)

IT 62229-50-9P, egf  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); USES (Uses) (platelet-derived; extn. of growth factors from tissue)

L31 ANSWER 21 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:489907 HCAPLUS

DOCUMENT NUMBER: 135:81959

TITLE: Gene transfer to intervertebral disc cells, and use in the treatment of degenerative disk disorders, and animal model for degenerative disk disease

INVENTOR(S): Kang, James D.; Evans, Christopher H.; Nishida, Kotaro; Robbins, Paul D.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                                                                                                                                                  | KIND                               | DATE     | APPLICATION NO. | DATE     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|----------|-----------------|----------|
| US 2001006948                                                                                                                                                                                                                                                                                                                                                                                                                                               | A1                                 | 20010705 | US 1998-199978  | 19981125 |
| PRIORITY APPLN. INFO.:                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                    |          | US 1998-199978  | 19981125 |
| AB Methods for transferring a gene to an intervertebral disk are disclosed. The methods find application in the treatment of patients for degenerative disk disorders, by use of a gene encoding a product that imparts a therapeutic and/or prophylactic benefit. The methods also find application in the establishment of an animal model for the study of degenerative disk disease. A genetically modified intervertebral disk cell is also disclosed. |                                    |          |                 |          |
| IC                                                                                                                                                                                                                                                                                                                                                                                                                                                          | ICM A61K048-00                     |          |                 |          |
| NCL                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 514044000                          |          |                 |          |
| CC                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 63-5 (Pharmaceuticals)             |          |                 |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Section cross-reference(s): 14     |          |                 |          |
| IT                                                                                                                                                                                                                                                                                                                                                                                                                                                          | <b>Bone morphogenetic proteins</b> |          |                 |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <b>Growth factors, animal</b>      |          |                 |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Interleukin 1 receptor antagonist  |          |                 |          |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                             | <b>Transforming growth factors</b> |          |                 |          |
| RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES                                                                                                                                                                                                                                                                                                       |                                    |          |                 |          |

(Uses)

(gene transfer to intervertebral disk cells, and use in treatment of degenerative disk disorders, and animal model for degenerative disk disease)

**IT Transforming growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.1-; gene transfer to intervertebral disk cells, and use in treatment of degenerative disk disorders, and animal model for degenerative disk disease)

**IT 61912-98-9, Insulin-like growth factor 62031-54-3,**

Fibroblast growth factor 86102-31-0, Tissue inhibitor of metalloproteinase 96282-35-8 105844-41-5, Plasminogen activator inhibitor

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(gene transfer to intervertebral disk cells, and use in treatment of degenerative disk disorders, and animal model for degenerative disk disease)

**IT 9015-73-0 10103-46-5, Calcium phosphate**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(gene transfer to intervertebral disk cells, and use in treatment of degenerative disk disorders, and animal model for degenerative disk disease)

L31 ANSWER 22 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:472523 HCAPLUS

DOCUMENT NUMBER: 135:66255

TITLE: Liquid composition of a biodegradable block copolymer for drug delivery system

INVENTOR(S): Seo, Min-hyo; Choi, In-ja

PATENT ASSIGNEE(S): Samyang Corp., S. Korea

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND                                                                                                                                                                                                                                                                                                                                                                       | DATE     | APPLICATION NO. | DATE     |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 2001045742 | A1                                                                                                                                                                                                                                                                                                                                                                         | 20010628 | WO 2000-KR1508  | 20001221 |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG                                                                                                                                                                                     |          |                 |          |
| EP 1244471    | A1                                                                                                                                                                                                                                                                                                                                                                         | 20021002 | EP 2000-989005  | 20001221 |
| R:            | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR                                                                                                                                                                                                                                                                     |          |                 |          |
| US 2003082234 | A1                                                                                                                                                                                                                                                                                                                                                                         | 20030501 | US 2002-169012  | 20020622 |



## PRIORITY APPLN. INFO.:

KR 1999-60349 A 19991222

WO 2000-KR1508 W 20001221

AB The present invention relates to a liq. polymeric compn. capable of forming a physiol. active substance-contg. implant when it is injected into a living body and a method of prepn. The compn. comprises a water-sol. biocompatible liq. polyethylene glycol deriv., a biodegradable block copolymer which is insol. in water but sol. in the water-sol. biocompatible liq. polyethylene glycol deriv. and a physiol. active substance. Thus, a triblock copolymer was prepd. from lactide-1,4-dioxanone and PEG. Piroxicam 150, the above biodegradable block copolymer 400, diacetyl polyethylene glycol 420, and gelatin 30 mg were dissolved in a 50% aq. HOAc soln. and the drug-contg. liq. polymeric compn. was filtered and the org. solvent was removed.

IC ICM A61K047-30

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 37

IT **Bone morphogenetic proteins**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(liq. compn. of biodegradable block copolymer for drug delivery system)

IT **Platelet-derived growth factors**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(liq. compn. of biodegradable block copolymer for drug delivery system)

IT 50-70-4, Sorbitol, biological studies 50-76-0, Actinomycin-D 50-78-2, Aspirin 50-99-7, Glucose, biological studies 51-21-8, 5-Fluorouracil 53-86-1, Indomethacin 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 59-01-8, Kanamycin 59-05-2, Methotrexate 59-23-4, Galactose, biological studies 60-54-8, Tetracycline 63-42-3, Lactose 69-53-4, Ampicillin 69-65-8, Mannitol 87-79-6, Sorbose 87-99-0, Xylitol 99-20-7, Trehalose 103-90-2, Acetaminophen 114-07-8, Erythromycin 151-21-3, Sodium dodecylsulfate, biological studies 471-34-1, Calcium carbonate, biological studies 557-34-6, Zinc acetate 564-25-0, Doxycycline 1066-17-7, colistin 1309-42-8, Magnesium hydroxide 1314-13-2, Zinc oxide, biological studies 1403-66-3, Gentamycin 1404-00-8, Mitomycin 1404-04-2, Neomycin 1404-90-6, Vancomycin 1405-87-4, bacitracin 1406-05-9, Penicillin 1407-47-2, angiotensin 3486-35-9, Zinc carbonate 5104-49-4, Flurbiprofen 6990-06-3, Fusidic acid 7446-70-0, Aluminum chloride, biological studies 7542-37-2, Paromomycin 7646-85-7, Zinc chloride, biological studies 7647-14-5, Sodium chloride, biological studies 7786-30-3, Magnesium chloride, biological studies 9001-63-2, Lysozyme 9002-72-6, Somatotropin 9003-39-8, Polyvinylpyrrolidone 9004-10-8, insulin, biological studies 9004-32-4, Sodium carboxymethyl cellulose 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9007-12-9, calcitonin 9007-92-5, glucagon, biological studies 9012-76-4, Chitosan 9034-39-3, growth hormone releasing factor 9034-40-6, LHRH 9061-61-4, nerve growth factor 10043-52-4, Calcium chloride, biological studies 10118-90-8, Minocycline 11056-06-7, Bleomycin 11096-26-7, erythropoietin 11111-12-9, Cephalosporin 12619-70-4, Cyclodextrin 13614-98-7, Minocycline hydrochloride 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15663-27-1, Cisplatin 15687-27-1, Ibuprofen 16039-53-5, Zinc lactate 20830-81-3, Daunorubicin 21645-51-2, Aluminum hydroxide, biological studies 22071-15-4, Ketoprofen 22204-53-1, Naproxen 23155-02-4, Phosphomycin 23214-92-8, Doxorubicin 24305-27-9, thyrotropin releasing hormone 25316-40-9, Adriamycin 25322-68-3D, alkyl ethers 25496-72-4, Glyceryl monooleate 29679-58-1, Fenoprofen 31566-31-1, Glyceryl monostearate 32986-56-4, Tobramycin 33069-62-4, Paclitaxel 34493-98-6, Dibekacin

36322-90-4, Piroxicam 37517-28-5, Amikacin 40828-46-4, Suprofen  
 41575-94-4, Carboplatin 51110-01-1, somatostatin 52093-21-7,  
 Micronomicin 53994-73-3, Cephaclo 58957-92-9, Idarubicin  
 59804-37-4, Tenoxicam 59995-64-1, Thienamycin 60118-07-2, endorphin  
**62229-50-9**, EGF 63527-52-6 64221-86-9, Imipenem 68767-14-6,  
 Loxoprofen 74011-58-8, Enoxacin 81627-83-0, M-CSF 82419-36-1,  
 Ofloxacin 85721-33-1, Ciprofloxacin 86090-08-6, angiostatin  
 100986-85-4, Levofloxacin 106392-12-5, Poloxamer 114977-28-5, Taxotere  
 126467-48-9, porcine growth hormone 143011-72-7, GCSF 187888-07-9,  
 endostatin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(liq. compn. of biodegradable block copolymer for drug delivery system)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 23 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:435269 HCAPLUS

DOCUMENT NUMBER: 135:56492

TITLE: Homologs of the **bone** morphogenetic protein  
 ligand chordin identified by sequence homology and  
 their uses

INVENTOR(S): Nakayama, Naoki; Wen, Duanzhi; Han, Chun-ya; He,  
 Ching; Yu, Dongyin

PATENT ASSIGNEE(S): Amgen, Inc., USA

SOURCE: PCT Int. Appl., 199 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND                                                                                                                                                                                                                                                                                                                                                                           | DATE     | APPLICATION NO. | DATE     |
|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 2001042465 | A2                                                                                                                                                                                                                                                                                                                                                                             | 20010614 | WO 2000-US32906 | 20001204 |
| WO 2001042465 | A3                                                                                                                                                                                                                                                                                                                                                                             | 20020124 |                 |          |
| W:            | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG                                                                                                                                                                                         |          |                 |          |
| EP 1238075    | A2                                                                                                                                                                                                                                                                                                                                                                             | 20020911 | EP 2000-980962  | 20001204 |
| R:            | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, IE, SI, LT, LV, FI, RO, MK, CY, AL                                                                                                                                                                                                                                                                                         |          |                 |          |

PRIORITY APPLN. INFO.: US 1999-169494P P 19991207  
 US 2000-724915 A 20001128  
 WO 2000-US32906 W 20001204

AB The present invention provides Chordin-Like (CHL) polypeptides and nucleic acid mols. encoding the same. The invention also provides selective binding agents, vectors, host cells, and methods for producing CHL polypeptides. The invention further provides pharmaceutical compns. and methods for the diagnosis, treatment, amelioration, and/or prevention of diseases, disorders, and conditions assocd. with CHL polypeptides. The mRNA for the protein is widely distributed in mouse and human tissues.

Translation of the mRNA for the mouse CHL protein in *Xenopus* oocytes indicated that it could antagonize the endogenous ventralizing factor about as efficiently as chordin.

- IC C12N015-12; C07K014-475; G01N033-53; C07K016-22; C12N005-12; A61K038-18; C12N015-86; C12N015-62; A01K067-027
- CC 2-10 (Mammalian Hormones)
- ST chordin like protein gene discovery human mouse sequence; **bone** morphogenetic protein antagonist chordin homolog gene discovery
- IT **Bone morphogenetic proteins**  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (4, CHL as ligand for; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Proteins, specific or class  
 RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)  
 (CHL (chordin-like); homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Immunoglobulins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (G, fusion products, with chordin-like proteins; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Nerve  
 (Purkinje cell, mRNA for chordin-like protein in; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Antibodies  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (anti-idiotypic, to CHL proteins; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Gene, animal  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (cDNA, for chordin-like protein; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Brain  
 (cerebral cortex, mRNA for chordin-like protein in; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Antibodies  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (chimeric, to CHL proteins; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Intestine  
 (colon, mucosa, mRNA for chordin-like protein in; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Polyoxyalkylenes, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (conjugates with chordin-like proteins; homologs of **bone**

morphogenetic protein ligand chordin identified by sequence homol. and their uses)

## IT mRNA

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)

(for chordin-like proteins, tissue distribution of; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)

## IT Drug screening

(for effectors of CHL proteins; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)

## IT Immunoglobulins

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(fragments, to CHL proteins; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)

## IT Genetic methods

(gene discovery; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)

## IT Molecular cloning

(homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)

## IT Chromosome

(human X, Xq22.1-23, gene for CHL protein mapping to; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)

## IT Antibodies

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(humanized, to CHL proteins; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)

## IT Adipose tissue

**Bone** marrow

Brain

Development, mammalian postnatal

Heart

Kidney

Liver

Lung

Lymph node

Muscle

Ovary

Prostate gland

Spleen

Testis

Thymus gland

(mRNA for chordin-like protein in; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)

## IT Antibodies

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(monoclonal, to CHL proteins; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)

## IT Chromosome

(mouse X, gene for CHL protein on; homologs of **bone**

- morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Genetic mapping  
(of gene for CHL protein of mouse and human; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Brain  
(olfactory bulb, external plexiform layer, mRNA for chordin-like protein in; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT **Bone**, disease  
(**osteopetrosis**, treatment of; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Alcohols, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(polyhydric, ethoxylated, conjugates with chordin-like proteins; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Mesenchyme  
(skin, mRNA for chordin-like protein in; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Intestine  
(small, mRNA for chordin-like protein in; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT Antibodies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(to CHL proteins; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT **Osteoporosis**  
(treatment of; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT 344972-07-2, Protein CHL (mouse clone 1-2) 344972-08-3 344972-09-4  
344972-10-7 344972-11-8 344972-13-0 344972-17-4 344972-18-5  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)  
(amino acid sequence; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT 344972-12-9 344972-14-1 344972-15-2 344972-16-3 344972-19-6  
344972-20-9 344972-21-0  
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(amino acid sequence; homologs of **bone** morphogenetic protein ligand chordin identified by sequence homol. and their uses)
- IT 57-55-6D, Propylene glycol, conjugates with chordin-like proteins  
9002-89-5D, Polyvinyl alcohol, conjugates with chordin-like proteins  
9003-11-6D, Propylene oxide ethylene oxide copolymer, conjugates with chordin-like proteins 9004-34-6D, Cellulose, conjugates with chordin-like proteins, biological studies 9004-54-0D, Dextran, conjugates with chordin-like proteins, biological studies 9004-74-4D, Monomethoxypolyethylene glycol, conjugates with chordin-like proteins  
25322-68-3D, Polyethylene glycol, conjugates with chordin-like proteins  
213329-63-6D, conjugates with chordin-like proteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (homologs of **bone** morphogenetic protein ligand chordin  
 identified by sequence homol. and their uses)

IT 344822-37-3 344822-38-4 344822-39-5 344822-40-8  
 RL: BSU (Biological study, unclassified); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (nucleotide sequence; homologs of **bone** morphogenetic protein  
 ligand chordin identified by sequence homol. and their uses)

IT 344972-25-4 344972-26-5 344972-27-6 344972-28-7 344972-29-8  
 344972-30-1 344972-31-2 344972-32-3 344972-33-4 344972-34-5  
 344972-35-6 344972-36-7 344972-37-8  
 RL: PRP (Properties)  
 (unclaimed nucleotide sequence; homologs of the **bone**  
 morphogenetic protein ligand chordin identified by sequence homol. and  
 their uses)

IT 217945-18-1, Chordin (mouse gene Chrd) 217945-19-2 344972-24-3  
 344972-38-9 344972-39-0 344972-40-3 344972-41-4  
 RL: PRP (Properties)  
 (unclaimed protein sequence; homologs of the **bone**  
 morphogenetic protein ligand chordin identified by sequence homol. and  
 their uses)

IT 191936-91-1 322644-80-4  
 RL: PRP (Properties)  
 (unclaimed sequence; homologs of the **bone** morphogenetic  
 protein ligand chordin identified by sequence homol. and their uses)

L31 ANSWER 24 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:416980 HCAPLUS

DOCUMENT NUMBER: 135:15095

TITLE: In situ bioreactors expressing systematically  
 available bioactive agents and methods of use thereof  
 in therapy

INVENTOR(S): Pierce, Glenn; Chandler, Lois Ann

PATENT ASSIGNEE(S): Selective Genetics, Inc., USA

SOURCE: PCT Int. Appl., 69 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2001040272 | A2   | 20010607 | WO 2000-US32754 | 20001130 |
| WO 2001040272 | A3   | 20020117 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001044413 A1 20011122 US 2000-729644 20001130

PRIORITY APPLN. INFO.: US 1999-168470P P 19991201

AB The present invention relates to a method of in vivo, sustained gene

therapy wherein one or more in situ bioreactors (or neo-organoids) express systematically available bioactive agents. One method involves implanting or placing into a tissue site a biocompatible substance capable of cellular ingrowth (e.g., device, matrix, semi-permeable membrane with a matrix or liq. interior, etc.). and systemic delivery of a bioactive factor. Also provided are compns., devices, and kits comprising the same. In various embodiments the biocompatible substance comprises a matrix and at least one nucleic acid mol. encoding a bioactive agent. In other embodiments bioreactors are provided wherein a first gene that encodes a growth factor is present and a second gene encoding a bioactive agent is present during manuf. or provided to the bioreactor following manuf. or implantation.

IC ICM C07K014-00

CC 3-2 (Biochemical Genetics)

Section cross-reference(s): 9, 63

IT **Platelet-derived growth factors**

RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PDGF-B, as cell growth stimulating agent; in situ bioreactors expressing systematically available bioactive agents and methods of use thereof in therapy)

IT Angiogenic factors

Antisense oligonucleotides

**Bone morphogenetic proteins**

Cell adhesion molecules

Chemotactic factors

Cytokines

Hepatocyte growth factor

Macrophage migration inhibitory factor

Ribozymes

**Transforming growth factors**

p53 (protein)

RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(as cell growth stimulating agent; in situ bioreactors expressing systematically available bioactive agents and methods of use thereof in therapy)

IT **Prosthetic materials and Prosthetics**

(bioactive glass, as biocompatible substance; in situ bioreactors expressing systematically available bioactive agents and methods of use thereof in therapy)

IT **Prosthetic materials and Prosthetics**

(ceramics, alumina, Bioceram, as biocompatible substance; in situ bioreactors expressing systematically available bioactive agents and methods of use thereof in therapy)

IT **Transforming growth factors**

RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(.beta.1-, as cell growth stimulating agent; in situ bioreactors expressing systematically available bioactive agents and methods of use thereof in therapy)

IT **Transforming growth factors**

RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(.beta.2-, as cell growth stimulating agent; in situ bioreactors expressing systematically available bioactive agents and methods of use thereof in therapy)

IT **Transforming growth factors**  
 RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (.beta.3-, as cell growth stimulating agent; in situ bioreactors expressing systematically available bioactive agents and methods of use thereof in therapy)

IT 9004-34-6, Cellulose, biological studies **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic acid 9012-76-4, chitosan  
 RL: BUU (Biological use, unclassified); DEV (Device component use); BIOL (Biological study); USES (Uses)  
 (as biocompatible substance (biol. matrix); in situ bioreactors expressing systematically available bioactive agents and methods of use thereof in therapy)

IT **61912-98-9P**, IGF **62031-54-3P**, FGF **62229-50-9P**, EGF 62683-29-8P, Colony-stimulating factor 127464-60-2P, Vascular endothelial growth factor 250740-90-0P, Angiopoietin  
 RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (as cell growth stimulating agent; in situ bioreactors expressing systematically available bioactive agents and methods of use thereof in therapy)

L31 ANSWER 25 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:50530 HCAPLUS

DOCUMENT NUMBER: 134:105921

TITLE: Human naturally secreted extracellular matrix-coated device

INVENTOR(S): Naughton, Gail K.; Zeltinger, Joan

PATENT ASSIGNEE(S): Advanced Tissue Sciences, Inc., USA

SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                                                                    | KIND | DATE     | APPLICATION NO. | DATE     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2001003750                                                                                                                                                                                                                                                                                                                                                                 | A1   | 20010118 | WO 2000-US18461 | 20000706 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG                                                                                                                                                                                        |      |          |                 |          |
| EP 1196206                                                                                                                                                                                                                                                                                                                                                                    | A1   | 20020417 | EP 2000-947054  | 20000706 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO                                                                                                                                                                                                                                                                                     |      |          |                 |          |

PRIORITY APPLN. INFO.: US 1999-350386 A 19990709

WO 2000-US18461 W 20000706

AB The present invention discloses compns. comprising a naturally secreted human extracellular matrix and methods for the use thereof. More particularly, the present invention provides compns. and methods for the repair of skin defects using natural human extracellular matrix by



injection. The present invention also provides prosthetic devices which are coated or sealed with a compn. comprising a naturally secreted extracellular matrix and methods for the use thereof. Fibroblast cells were cultured on a three-dimensional framework and in monolayer tissue culture dishes. The amt. of collagen synthesized per cell in three-dimensional frame work was 26-116 ng/106 as compared with 6.5-16 ng/106/day for monolayer cultures.

IC ICM A61L027-36  
ICS A61L027-34  
CC 63-7 (Pharmaceuticals)  
Section cross-reference(s): 38  
IT **Bone marrow**  
Chondrocyte  
Epithelium  
Extracellular matrix  
Fibroblast  
Leukocyte  
Lubricants  
Macrophage  
Mast cell  
Monocyte  
Sponge (Porifera)  
Transplant and Transplantation  
(human naturally secreted extracellular matrix-coated device)  
IT **Growth factors, animal**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(human naturally secreted extracellular matrix-coated device)  
IT **Prosthetic materials and Prosthetics**  
(implants, vascular; human naturally secreted extracellular matrix-coated device)  
IT **Prosthetic materials and Prosthetics**  
(implants; human naturally secreted extracellular matrix-coated device)  
IT 97-90-5, Ethylene glycol dimethacrylate 9002-84-0, Polytetrafluoroethylene 9002-88-4, Polyethylene 9003-07-0, Polypropylene 9003-53-6, Polystyrene 9004-34-6, Cellulose, biological studies **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic acid 9004-70-0, Nitrocellulose 9005-32-7, Alginic acid 9011-14-7, Polymethylmethacrylate 9012-76-4, Chitosan 9016-00-6, Poly[oxy(dimethylsilylene)] 24980-41-4, Poly(.epsilon.-caprolactone 25038-59-9, Polyethyleneterephthalate, biological studies 25189-52-0, Poly(.gamma.-ethyl glutamate 25248-42-4, Poly[oxy(1-oxo-1,6-hexanediyl)] 25249-16-5, Poly 2-hydroxyethyl methacrylate 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26063-00-3, Poly(.beta.-hydroxybutyrate 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 26780-50-7, Polyglycolide-lactide 31621-87-1, Polydioxanone 33410-59-2, Poly HEMA  
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(human naturally secreted extracellular matrix-coated device)  
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT  
L31 ANSWER 26 OF 43 HCAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2000:900497 HCAPLUS  
DOCUMENT NUMBER: 134:61577

TITLE: Biologically active material based on an insolubilized dextran derivative and a growth factor

INVENTOR(S): Blanchat, Cinderella; Logeart-avramoglou, Delphine; Petite, Herve; Meunier, Alain; Chaubet, Frederic; Jozefonvicz, Jacqueline; Jozefowicz, Marcel; Sedel, Laurent; Correia, Jose

PATENT ASSIGNEE(S): Iterfi, Fr.

SOURCE: PCT Int. Appl., 42 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                 | KIND | DATE     | APPLICATION NO. | DATE       |
|----------------------------------------------------------------------------|------|----------|-----------------|------------|
| WO 2000076562                                                              | A1   | 20001221 | WO 2000-FR1603  | 20000609   |
| W: CA, JP, US                                                              |      |          |                 |            |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE |      |          |                 |            |
| FR 2794649                                                                 | A1   | 20001215 | FR 1999-7401    | 19990611   |
| FR 2794649                                                                 | B1   | 20030411 |                 |            |
| EP 1189644                                                                 | A1   | 20020327 | EP 2000-940481  | 20000609   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI  |      |          |                 |            |
| JP 2003501217                                                              | T2   | 20030114 | JP 2001-502893  | 20000609   |
| US 2002169120                                                              | A1   | 20021114 | US 2001-16706   | 20011211   |
| PRIORITY APPLN. INFO.:                                                     |      |          |                 |            |
|                                                                            |      |          | FR 1999-7401    | A 19990611 |
|                                                                            |      |          | WO 2000-FR1603  | W 20000609 |

AB The invention concerns a biol. active material essentially comprising at least an insolubilized dextran deriv. of general formula DMCaBbSucSd and at least a growth factor having an activity on **osteoarticular, dental** and/or **maxillofacial** tissues, and the method for prepg. same. The invention also concerns the uses of said biomaterial for prepg. a repair or filling material, such as an implant, for **osteoarticular, dental** or **maxillofacial** applications and for prepg. an orthopedic, **dental** or **maxillofacial** prosthesis, and the prosthesis coated with said biol. active material. A hydrogel comprising dextran derivs. crosslinked with sodium trimetaphosphate and 0.5 ng/gel **bone** morphogenic protein was prepd. and lyophilized to obtain a powder. Thus, 15 mg of the above powder was rehydrated with 100 .mu.L water and used as a **bone** implant to fill a **bone** cavity of about 50 mm<sup>3</sup>.

IC ICM A61L027-54

ICS A61L027-22; A61L027-20; A61L027-26; A61L027-48; A61L027-46

CC 63-7 (Pharmaceuticals)

IT **Bone formation**

Coral

Crosslinking agents

**Dental materials and appliances**

**Prosthetic materials and Prosthetics**

Tooth

(biol. active material based on insolubilized dextran deriv. and growth factor)

IT **Bone morphogenetic proteins**

**Growth factors, animal**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(biol. active material based on insolubilized dextran deriv. and growth factor)

IT **Prosthetic materials and Prosthetics**

(implants; biol. active material based on insolubilized dextran deriv. and growth factor)

IT **Prosthetic materials and Prosthetics**

(orthopedic; biol. active material based on insolubilized dextran deriv. and growth factor)

IT 1306-06-5, Hydroxyapatite 7758-87-4, Tricalcium phosphate  
**9004-54-0D**, Dextran, derivs., biological studies 25322-68-3,  
 Polyethylene glycol 26009-03-0, Polyglycolic acid 26124-68-5,  
 Polyglycolic acid 34346-01-5, Glycolic acid lactic acid copolymer  
 RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(biol. active material based on insolubilized dextran deriv. and growth factor)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 27 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:790360 HCAPLUS

DOCUMENT NUMBER: 133:355218

TITLE: Gene therapy using TGF-.beta.

INVENTOR(S): Noh, Moon Jong; Kang, Kyoung Ae; Lee, Kwan Hee

PATENT ASSIGNEE(S): Kolon Industries, Inc., S. Korea

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND                                                                                                                                                                                                                                                                                                                                                       | DATE     | APPLICATION NO. | DATE     |
|---------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 2000066177 | A1                                                                                                                                                                                                                                                                                                                                                         | 20001109 | WO 2000-IB653   | 20000503 |
| W:            | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG                                                                                                                                                                             |          |                 |          |
| KR 2000072904 | A                                                                                                                                                                                                                                                                                                                                                          | 20001205 | KR 1999-15854   | 19990503 |
| US 6315992    | B1                                                                                                                                                                                                                                                                                                                                                         | 20011113 | US 1999-345415  | 19990630 |
| EP 1175228    | A1                                                                                                                                                                                                                                                                                                                                                         | 20020130 | EP 2000-925522  | 20000503 |
| R:            | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO                                                                                                                                                                                                                                                                     |          |                 |          |

PRIORITY APPLN. INFO.: KR 1999-15854 A 19990503  
 US 1999-345415 A 19990630  
 WO 2000-IB653 W 20000503

AB The subject invention is related to a cell-mediated gene therapy treatment for orthopedic disease using a member belonging to the transforming growth factor-.beta. (TGF-.beta.) superfamily. TGF-.beta. gene therapy as a new

treatment method for degenerative arthritis is demonstrated. After transfection of TGF- $\beta$ . cDNA expression vectors into fibroblasts (NIH 3T3-TGF- $\beta$ .1), the cells were injected into rabbit Achilles tendon and knee joints with artificially-made cartilage defects. Intratendinous injections were performed to det. the optimal concn. for in vivo expression. Partially defected cartilage model was made to simulate degenerative arthritis of the knee joint. The partial cartilage defect treated with the cell-mediated gene therapy procedure was covered by newly formed hyaline cartilage which indicates that the cells survived and stimulated matrix formation in this area. Completely denuded cartilage areas were covered by fibrous collagen.

- IC ICM A61K048-00  
ICS C12N015-09; C12N015-63; C07K014-95  
CC 63-5 (Pharmaceuticals)  
Section cross-reference(s): 15
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(2; antiarthritic gene therapy using TGF- $\beta$ .)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(3; antiarthritic gene therapy using TGF- $\beta$ .)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(4; antiarthritic gene therapy using TGF- $\beta$ .)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(5; antiarthritic gene therapy using TGF- $\beta$ .)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(6; antiarthritic gene therapy using TGF- $\beta$ .)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(7; antiarthritic gene therapy using TGF- $\beta$ .)
- IT Antiarthritics  
Cartilage  
Chondrocyte  
Electroporation  
Fibroblast  
Gene therapy  
Joint, anatomical  
Ligament  
Mesenchyme  
Molecular cloning  
**Osteoblast**  
Plasmid vectors

Tendon  
Transformation, genetic  
Transplant and Transplantation  
Virus vectors  
(antiarthritic gene therapy using TGF-.beta.)

**IT Transforming growth factors**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(genes encoding; antiarthritic gene therapy using TGF-.beta.)

**IT Transforming growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.-; antiarthritic gene therapy using TGF-.beta.)

**IT Transforming growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.1-; antiarthritic gene therapy using TGF-.beta.)

**IT Transforming growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.2-; antiarthritic gene therapy using TGF-.beta.)

**IT Transforming growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.3-; antiarthritic gene therapy using TGF-.beta.)

**IT 9015-73-0**

RL: NUU (Other use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiarthritic gene therapy using TGF-.beta.)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 28 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:513547 HCAPLUS

DOCUMENT NUMBER: 133:125280

TITLE: Compositions and methods for controlled delivery of virus vectors

INVENTOR(S): Levy, Robert J.; Jones, Peter L.

PATENT ASSIGNEE(S): Children's Hospital of Philadelphia, USA

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND                                                                                                                                                                                                                                                                                                                            | DATE     | APPLICATION NO. | DATE     |
|---------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 2000043044 | A1                                                                                                                                                                                                                                                                                                                              | 20000727 | WO 2000-US1193  | 20000119 |
| W:            | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, |          |                 |          |

AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-116405P P 19990119

AB The invention relates to compns. and methods for delivering a virus vector to an animal. The compns. include compns. which comprise a matrix having a virus vector bound at the exterior surface thereof in a physiol. reversible manner. The invention also includes methods of making such compns., including particles, devices, bulk materials, and other objects which comprise, consist of, or are coated with such compns. Methods of delivering a virus vector to an animal tissue are also described.

IC ICM A61K048-00

ICS C12N015-63; A61B019-00; C07H021-04

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 3

IT **Platelet-derived growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(-.beta.; compns. and methods for controlled delivery of virus vectors)

IT **Bone morphogenetic proteins**

**Platelet-derived growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(compns. and methods for controlled delivery of virus vectors)

IT **Transforming growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(.beta.-; compns. and methods for controlled delivery of virus vectors)

IT 9002-06-6, Thymidine kinase 9002-64-6, Pth 9002-72-6, Somatotropin

**61912-98-9**, Insulin like growth factor **62031-54-3**, Fgf

139639-23-9, Tissue plasminogen activator

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(compns. and methods for controlled delivery of virus vectors)

IT 97-90-5, Ethylene glycol dimethacrylate 108-05-4D, Vinyl acetate, copolymers 1306-06-5, Hydroxyapatite 6606-65-1 7440-06-4, Platinum, biological studies 7440-32-6, Titanium, biological studies 7758-87-4, Tricalcium phosphate 9002-84-0, Polytetrafluoroethylene 9002-86-2, Polyvinyl chloride 9002-88-4, Polyethylene 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-07-0, Polypropylene 9003-17-2, Polybutadiene 9003-18-3 9003-20-7, Vinyl acetate homopolymer 9003-27-4, Polyisobutylene 9003-31-0, Polyisoprene 9003-39-8, Polyvinylpyrrolidone 9003-53-6, Polystyrene 9003-54-7, PolyStyrene acrylonitrile 9003-56-9 9004-35-7, Cellulose acetate 9004-53-9, Dextrin **9004-54-0**, Dextran, biological studies 9005-32-7, Alginic acid 9011-14-7, Polymethylmethacrylate 9012-36-6, Agarose 9016-80-2, Polymethylpentene 9017-21-4, Polymethylstyrene 9046-31-5, Polystyrene carboxylic acid 10586-17-1, Isopropyl cyanoacrylate 12597-68-1, Stainless steel, biological studies 15802-18-3D, polyalkyl derivs. 21982-30-9, Hydroxymethyl methacrylate 24937-78-8, Ethylene vinyl acetate copolymer 24980-41-4, Polycaprolactone 24981-14-4, Polyvinyl fluoride 25014-41-9, Polyacrylonitrile 25068-26-2,

Polymethylpentene 25087-26-7, Polymethacrylic acid 25102-52-7,  
 Butadiene-isoprene copolymer 25248-42-4, Polycaprolactone 26009-03-0,  
 Polyglycolic acid 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)]  
 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 34346-01-5,  
 Glycolic acid-lactic acid copolymer 50851-57-5, Polystyrene sulfonic  
 acid 61128-18-5, Caprolactone glycolic acid copolymer

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic  
 use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (controlled-delivery matrix; compns. and methods for controlled  
 delivery of virus vectors)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 29 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:493334 HCAPLUS

DOCUMENT NUMBER: 133:125276

TITLE: Sustained delivery of polyionic bioactive agents

INVENTOR(S): Levy, Robert J.

PATENT ASSIGNEE(S): The Children's Hospital of Philadelphia, USA

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2000041647                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | A1   | 20000720 | WO 2000-US1317  | 20000119 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,<br>CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,<br>IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,<br>MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,<br>SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,<br>AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,<br>DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,<br>CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG |      |          |                 |          |
| US 6395029                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | B1   | 20020528 | US 1999-234011  | 19990119 |

PRIORITY APPLN. INFO.: US 1999-234011 A 19990119

AB The invention relates to compns. and methods for delivering a polyionic  
 bioactive compn. such as a nucleic acid to a tissue of an animal. The  
 compns. of the invention include compns. which comprise a matrix  
 comprising the polyionic bioactive agent and wherein at least most of the  
 polyionic bioactive agent at the exterior portion of the matrix is present  
 in a condensed form. The invention also includes methods of making such  
 compns., including particles, devices, bulk materials, and other objects  
 which comprise, consist of, or are coated with such compns. Methods of  
 delivering a polyionic bioactive agent to an animal tissue are also  
 described. The invention further includes a method of storing a nucleic  
 acid.

IC ICM A61F002-02

ICS A61F002-06; A61F013-00; A61K009-14; A61K009-16; A61K009-127;  
 A61K047-00; A61K047-48

CC 63-5 (Pharmaceuticals)

IT Drug delivery systems

**Prosthetic materials and Prosthetics**

(implants; sustained delivery of nucleic acids and other polyionic bioactive agents)

IT Antisense oligonucleotides

**Bone morphogenetic proteins**

Cocoa butter

DNA

Ethylene-propylene rubber

Fluoropolymers, biological studies

Neoprene rubber, biological studies

Nitrile rubber, biological studies

**Platelet-derived growth factors**

Polyamides, biological studies

Polyanhydrides

Polycarbonates, biological studies

Polyesters, biological studies

Polyimides, biological studies

Polyoxyalkylenes, biological studies

Polysulfones, biological studies

Polyurethanes, biological studies

RNA

Rayon, biological studies

Ribozymes

Silicone rubber, biological studies

Stem cell factor

Waxes

cDNA

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(sustained delivery of nucleic acids and other polyionic bioactive agents)

IT **Transforming growth factors**

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(.beta.-; sustained delivery of nucleic acids and other polyionic bioactive agents)

- IT 97-90-5, Ethylene glycol dimethacrylate 1306-06-5, Hydroxyapatite 6606-65-1 7440-06-4, Platinum, biological studies 7440-32-6, Titanium, biological studies 7758-87-4, Tricalcium phosphate 9002-06-6, Thymidine kinase 9002-64-6, Pth 9002-72-6, Growth hormone 9002-84-0, Polytetrafluoroethylene 9002-86-2, Polyvinyl chloride 9002-88-4, Polyethylene 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-07-0, Polypropylene 9003-17-2, Polybutadiene 9003-18-3, Acrylonitrile butadiene copolymer 9003-20-7, Polyvinylacetate 9003-27-4, Polyisobutylene 9003-31-0, Polyisoprene 9003-39-8, Polyvinylpyrrolidone 9003-42-3, Polyethylmethacrylate 9003-53-6, Polystyrene 9003-56-9, Acrylonitrile butadiene styrene copolymer 9004-35-7, Cellulose acetate 9004-53-9, Dextrin **9004-54-0**, Dextran, biological studies 9005-32-7, Alginic acid 9011-14-7, Polymethylmethacrylate 9012-36-6, Agarose 9016-80-2, Polymethylpentene 9017-21-4, Polymethylstyrene 9046-31-5, Polystyrene carboxylic acid 10586-17-1, Isopropyl cyanoacrylate 12597-68-1, Stainless steel, biological studies 15802-18-3D, Cyanoacrylic acid, polyalkyl derivs. 21982-30-9, Hydroxymethyl methacrylate 24937-78-8, Ethylene vinyl acetate copolymer 24980-41-4, Polycaprolactone 24981-14-4, Polyvinyl fluoride 25068-26-2, Polymethylpentene 25087-26-7, Polymethacrylic acid 25102-52-7, Butadiene-isoprene copolymer 25248-42-4, Polycaprolactone 26009-03-0, Polyglycolic acid 26023-30-3,



Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid  
 26124-68-5, Polyglycolic acid 50851-57-5, Polystyrene sulfonic acid  
 61128-18-5, Caprolactone-glycolic acid copolymer **61912-98-9**,  
 Insulin-like growth factor **62031-54-3**, Fgf 80137-67-3,  
 Caprolactone-lactic acid copolymer 139639-23-9, Tissue plasminogen  
 activator

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic  
 use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (sustained delivery of nucleic acids and other polyionic bioactive  
 agents)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 30 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:141482 HCAPLUS

DOCUMENT NUMBER: 132:185482

TITLE: Malleable paste for filling **bone** defects

INVENTOR(S): Gertzman, Arthur A.; Sunwoo, Moon Hae

PATENT ASSIGNEE(S): Musculoskeletal Transplant Foundation, USA

SOURCE: U.S., 7 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

| PATENT NO.                                                                                   | KIND | DATE     | APPLICATION NO. | DATE        |
|----------------------------------------------------------------------------------------------|------|----------|-----------------|-------------|
| US 6030635                                                                                   | A    | 20000229 | US 1998-31750   | 19980227    |
| US 6326018                                                                                   | B1   | 20011204 | US 1999-413815  | 19991007    |
| EP 1127581                                                                                   | A1   | 20010829 | EP 2000-301370  | 20000222    |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,<br>IE, SI, LT, LV, FI, RO |      |          |                 |             |
| US 6437018                                                                                   | B1   | 20020820 | US 2000-515656  | 20000229    |
| US 6458375                                                                                   | B1   | 20021001 | US 2000-677891  | 20001003    |
| PRIORITY APPLN. INFO.:                                                                       |      |          | US 1998-31750   | A3 19980227 |
|                                                                                              |      |          | US 1999-365880  | B2 19990803 |
|                                                                                              |      |          | US 2000-515656  | A2 20000229 |

AB The invention is directed toward a malleable **bone** putty and a flowable gel compn. for application to a **bone** defect site to promote new **bone** growth at the site which comprises a new **bone** growth inducing compd. of demineralized lyophilized allograft **bone** powder. The **bone** powder has a particle size ranging from about 100 to about 850 .mu. and is mixed in a high mol. wt. hydrogel carrier, the hydrogel component of the carrier ranging from 0.3 to 3.0% of the compn. and having a mol. wt. of about at least 10,000 Daltons. The compn. contains about 25% to about 40% **bone** powder and can be addnl. provided with BMP's and a sodium phosphate buffer. A malleable putty of 2% soln. hyaluronic acid in isotonic saline with 250-420 .mu. cortical allograft **bone** powder at 30%. Freeze dried cortical allograft **bone** (502 mg) of particle size ranging 250-420 .mu. was mixed into 1170 mg of a 2% soln. of sodium hyaluronate in isotonic saline. The **bone** component is added to achieve a **bone** concn. of 30% (wt./wt.). The soln. was well mixed and allowed to stand for 2-3 h at room temp. to provide a malleable putty with excellent formability properties.

IC ICM A61L025-00

ICS A61L015-64; A61K035-32  
 NCL 424423000  
 CC 63-7 (Pharmaceuticals)  
 ST antibiotic **bone** defect filling paste  
 IT **Bone**, disease  
     (defect; malleable paste for filling **bone** defects)  
 IT Antibiotics  
     Antimicrobial agents  
         **Bone formation**  
         Particle size distribution  
             (malleable paste for filling **bone** defects)  
 IT **Bone morphogenetic proteins**  
     Enzymes, biological studies  
     Vitamins  
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
         (malleable paste for filling **bone** defects)  
 IT **Bone**  
     (powders; malleable paste for filling **bone** defects)  
 IT 56-75-7, Chloromycetin 57-92-1, biological studies 60-54-8,  
     Tetracycline 69-53-4, Ampicillin 114-07-8, Erythromycin 1306-06-5,  
     Hydroxylapatite (Ca<sub>5</sub>(OH)(PO<sub>4</sub>)<sub>3</sub>) 1403-66-3, Gentamicin 1404-04-2,  
     Neomycin 1404-26-8, Polymyxin B 1405-87-4, Bacitracin 1406-05-9,  
     Penicillin 7440-70-2D, Calcium, salts, biological studies 7758-87-4,  
     Calcium phosphate 7778-18-9 9001-12-1, Collagenase **9004-54-0**  
     , Dextran, biological studies 9004-61-9, Hyaluronic acid 9012-76-4,  
     Chitosan 9031-96-3, Peptidase 9035-73-8, Oxidase 9067-32-7, Sodium  
     hyaluronate 10043-52-4, Calcium chloride (CaCl<sub>2</sub>), biological studies  
     18323-44-9, Clindamycin 25953-19-9, Cefazolin 32986-56-4 32988-50-4,  
     Viomycin 104184-69-2, Azactam 106392-12-5, Pluronic 107043-88-9,  
     N,O-Carboxymethyl chitosan  
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
         (malleable paste for filling **bone** defects)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 31 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:686567 HCAPLUS

DOCUMENT NUMBER: 131:303417

TITLE: Collagen-polysaccharide matrix for **bone** and  
 cartilage repair

INVENTOR(S): Liu, Linshu; Spiro, Robert

PATENT ASSIGNEE(S): Orquest, Inc., USA

SOURCE: U.S., 10 pp., Cont.-in-part of U.S. 5,866,165.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE        |
|------------------------|------|----------|-----------------|-------------|
| US 5972385             | A    | 19991026 | US 1998-7731    | 19980115    |
| US 5866165             | A    | 19990202 | US 1997-783650  | 19970115    |
| US 6309670             | B1   | 20011030 | US 1999-324792  | 19990603    |
| PRIORITY APPLN. INFO.: |      |          | US 1997-783650  | A2 19970115 |
|                        |      |          | US 1998-7731    | A2 19980115 |

AB A matrix and a method for prepg. it are provided to support the growth of

tissue, such as **bone**, cartilage or soft tissue. A polysaccharide is reacted with an oxidizing agent to open sugar rings on the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent linkages to collagen. Collagen-hyaluronate conjugates were prepd. according to above method using sodium periodate. Above conjugate matrix was implanted into a 5 mm by 3 mm defect created in the parietal **bone** of rats. All matrix-filled defects were completely radiodense after 28 days, with no distinctive defect borders, which indicated complete healing. Unfilled defects appeared as ovoid radiolucent areas with rounded corners, suggesting minimal healing.

- IC ICM A61K038-39
- ICS A61K009-10; A61K047-42; A61K047-36
- NCL 424486000
- CC 63-7 (Pharmaceuticals)
- ST collagen polysaccharide matrix **bone** cartilage repair
- IT Drying
  - (air; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Freeze drying
  - Freezing
  - (collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT **Bone morphogenetic proteins**
  - Interleukins
  - Platelet-derived growth factors**
  - Proteins, general, biological studies
  - RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
  - (collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Fibrinogens
  - RL: BSU (Biological study, unclassified); BIOL (Biological study)
  - (collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Collagens, biological studies
  - RL: DEV (Device component use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
  - (conjugates with polysaccharides; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Polysaccharides, biological studies
  - RL: DEV (Device component use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
  - (conjugates, with collagen; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT **Bone**, disease
  - (defect; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT **Bone**
  - Cartilage
  - (repair; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Animal tissue
  - (soft; collagen-polysaccharide matrix for **bone** and cartilage repair)

- IT Collagens, biological studies  
 RL: DEV (Device component use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (type I, conjugates with polysaccharides; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Collagens, biological studies  
 RL: DEV (Device component use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (type II, conjugates with polysaccharides; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT **Transforming growth factors**  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (.beta.-; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT **61912-98-9**, Insulin-like growth factor **62031-54-3**, Fibroblast growth factor 62683-29-8, Colony-stimulating factor 173247-99-9  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT 7790-28-5, Sodium periodate.  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT **9004-54-ODP**, Dextran, conjugates with with collagen, biological studies 9004-61-9DP, Hyaluronic acid, conjugates with with collagen 9005-32-7DP, Alginic acid, conjugates with with collagen 9007-28-7DP, Chondroitin sulfate, conjugates with with collagen 9042-14-2DP, Dextran sulfate, conjugates with with collagen 9050-30-ODP, Heparan sulfate, conjugates with with collagen 9056-36-4DP, Keratan sulfate, conjugates with with collagen 70226-44-7DP, Heparan, conjugates with with collagen  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (collagen-polysaccharide matrix for **bone** and cartilage repair)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 32 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:249066 HCAPLUS

DOCUMENT NUMBER: 130:287100

TITLE: Hydraulic surgical cements comprising calcium phosphate

INVENTOR(S): Lemaitre, Jaques; Bohner, Marc; Van Landuyt, Pascale

PATENT ASSIGNEE(S): H. C. Robert Mathys Stiftung, Switz.; Stratec Medical A.-G.

SOURCE: PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

| PATENT NO.                                                                 | KIND | DATE     | APPLICATION NO. | DATE     |
|----------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 9917710                                                                 | A1   | 19990415 | WO 1998-EP6330  | 19981006 |
| W: CA, JP, US                                                              |      |          |                 |          |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE |      |          |                 |          |
| CA 2306562                                                                 | AA   | 19990415 | CA 1998-2306562 | 19981006 |
| EP 1023032                                                                 | A1   | 20000802 | EP 1998-954344  | 19981006 |
| EP 1023032                                                                 | B1   | 20020102 |                 |          |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, MC, PT, IE, FI      |      |          |                 |          |
| JP 2001518359                                                              | T2   | 20011016 | JP 2000-514603  | 19981006 |
| AT 211379                                                                  | E    | 20020115 | AT 1998-954344  | 19981006 |
| ES 2170533                                                                 | T3   | 20020801 | ES 1998-954344  | 19981006 |
| US 6425949                                                                 | B1   | 20020730 | US 2000-529054  | 20000707 |

## PRIORITY APPLN. INFO.:

WO 1997-EP5495 A 19971007  
 WO 1998-EP6330 W 19981006

- AB The cement for surgical purposes comprises three components. The first component comprises .beta.-Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub> (.beta.-TCP) particles; and Ca(H<sub>2</sub>PO<sub>4</sub>)<sub>2</sub> (MCPA) or Ca(H<sub>2</sub>PO<sub>4</sub>)<sub>2</sub>.cntdot.H<sub>2</sub>O (MCPM) particles or phosphoric acid. The second component comprises water. The third component comprises particles having an av. diam. which is larger than the av. diam. of the .beta.-TCP particles of the first component. Upon mixing of the three components a hardened mass comprising brushite CaHPO<sub>4</sub>.cntdot.2H<sub>2</sub>O (DCPD) is formed. The .beta.-TCP particles have a sp. surface area of less than 10,000 m<sup>2</sup>/g and a Ca/P at. ratio different from 1.50. The component constitutes 1-99 % of the hardened mass. The cements according to the invention may be used in **dental** and **maxillofacial** surgery (alveolar ridge reconstruction, **dental** socket filling), for orthopedic applications (**bone** fracture repair, **bone** augmentation) and for local drug delivery (antibiotics, anti-inflammatory and anti-cancer drugs).
- IC ICM A61K006-033  
 ICS A61L025-00; A61L027-00
- CC 63-7 (Pharmaceuticals)
- ST surgical cement calcium phosphate biodegradable polymer; **dental** cement calcium phosphate biodegradable polymer
- IT **Bone**  
 (artificial, for temporary use; hydraulic surgical cements comprising calcium phosphate and setting-rate controller and biodegradable polymers)
- IT **Growth factors, animal**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (**bone**-derived, for drug delivery; hydraulic surgical cements comprising calcium phosphate and setting-rate controller and biodegradable polymers)
- IT **Dental materials and appliances**  
 Medical goods  
 (cements; hydraulic surgical cements comprising calcium phosphate and setting-rate controller and biodegradable polymers)
- IT **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic acid 9004-65-3, Hydroxypropyl methyl cellulose 9012-36-6, Agarose 9012-76-4, Chitosan 11138-66-2, Xanthan gum 25249-16-5 25322-68-3  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (hydraulic surgical cements comprising calcium phosphate and setting-rate controller and biodegradable polymers)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 33 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:222847 HCAPLUS

DOCUMENT NUMBER: 130:257353

TITLE: Inorganic-polymer complexes for the controlled release of compounds including medicinals

INVENTOR(S): Royer, Garfield P.

PATENT ASSIGNEE(S): Buford Biomedical, Inc., USA

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                        | KIND | DATE     | APPLICATION NO. | DATE     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 9915150                                                                                                                                                                                                                                                                                                                        | A1   | 19990401 | WO 1998-US19528 | 19980922 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG                                                                                                                                                        |      |          |                 |          |
| US 6391336                                                                                                                                                                                                                                                                                                                        | B1   | 20020521 | US 1997-935300  | 19970922 |
| CA 2303884                                                                                                                                                                                                                                                                                                                        | AA   | 19990401 | CA 1998-2303884 | 19980922 |
| AU 9894925                                                                                                                                                                                                                                                                                                                        | A1   | 19990412 | AU 1998-94925   | 19980922 |
| EP 1017364                                                                                                                                                                                                                                                                                                                        | A1   | 20000712 | EP 1998-948335  | 19980922 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO                                                                                                                                                                                                                                         |      |          |                 |          |
| JP 2001517613                                                                                                                                                                                                                                                                                                                     | T2   | 20011009 | JP 2000-512521  | 19980922 |
| PRIORITY APPLN. INFO.: US 1997-935300 A2 19970922                                                                                                                                                                                                                                                                                 |      |          |                 |          |
| WO 1998-US19528 W 19980922                                                                                                                                                                                                                                                                                                        |      |          |                 |          |

AB This invention relates generally to the prodn. and use of inorg.-polymer complexes for the controlled release of compds. including medicinals. Advantageously, the inorg. used is calcium sulfate. CaSO<sub>4</sub> 1000, norfloxacin 50, and iodipamide 110 mg, all finely ground, were mixed and to this mixt. was added 0.6 mL of hyaluronic acid soln. (2 %). The slurry was mixed and loaded into the barrel of a syringe for administration or casting in a mold.

IC ICM A61K009-00

ICS A61K009-36

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 5

IT **Bone**, disease

(defect; drug delivery systems contg. inorg. compds. and matrix polymers and complexing agents)

IT **Bone morphogenetic proteins**

Glycosaminoglycans, biological studies

**Growth factors, animal**

Lecithins

Lipids, biological studies

Pheromones, animal

Polynucleotides

Polyoxyalkylenes, biological studies

Proteins, general, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug delivery systems contg. inorg. compds. and matrix polymers and complexing agents)

IT 50-03-3, Hydrocortisone acetate 50-23-7 57-27-2, Morphine, biological studies 57-88-5, Cholest-5-en-3-ol (3.beta.)-, biological studies 59-46-1, Procaine 87-08-1, Penicillin V 112-38-9, 10-Undecenoic acid 124-07-2, Octanoic acid, biological studies 133-16-4, Chloroprocaine 137-58-6, Lidocaine 140-28-3, Benzathine 147-52-4, Nafcillin 154-21-2, Lincomycin 466-99-9, Hydromorphone 606-17-7, Iodipamide 721-50-6, Prilocaine 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1403-66-3, Gentamicin 1404-90-6, Vancomycin 1406-05-9, Penicillin 1406-11-7, Polymyxin 2203-97-6, Hydrocortisone succinate 6678-14-4 7585-39-9D, .beta.-Cyclodextrin, hydroxypropyl ethers 7778-18-9, Calcium sulfate 9002-89-5, Polyvinyl alcohol 9002-98-6 9003-01-4, Polyacrylic acid 9003-39-8, PVP 9003-47-8, Polyvinylpyridine 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid 9005-65-6, Polysorbate 80 9007-28-7, Chondroitin sulfate 9042-14-2, Dextran sulfate 10118-90-8, Minocycline 11138-66-2, Xanthan gum 15663-27-1, cis-Platin 15686-71-2, Cephalexin 22199-08-2, Silver sulfadiazine 24991-23-9 25322-68-3 25513-46-6, Polyglutamic acid 25608-40-6, Polyaspartic acid 25953-19-9, Cefazolin 26063-13-8, Polyaspartic acid 26336-38-9, Polyvinylamine 26913-06-4, Poly[imino(1,2-ethanediyl)] 36637-18-0, Etidocaine 37517-28-5, Amikacin 38396-39-3, Bupivacaine 39831-55-5, Amikacin sulfate 52580-78-6, Polymyxin sulfate 53648-55-8, Dezocine 61477-96-1, Piperacillin 64221-86-9, Imipenem 70458-96-7, Norfloxacin 81103-11-9, Clarithromycin 85721-33-1, Ciprofloxacin 93106-60-6, Enrofloxacin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug delivery systems contg. inorg. compds. and matrix polymers and complexing agents)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 34 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:48632 HCAPLUS

DOCUMENT NUMBER: 130:100691

TITLE: Crosslinked polysaccharide drug carrier

INVENTOR(S): Spiro, Robert C.; Thompson, Andrea Y.; Liu, Linshu

PATENT ASSIGNEE(S): Orquest, Inc., USA

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                         | KIND | DATE     | APPLICATION NO. | DATE     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 9901143                                                                                                                                                                                         | A1   | 19990114 | WO 1998-US13997 | 19980701 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, |      |          |                 |          |

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
 UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
 CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9882909 A1 19990125 AU 1998-82909 19980701

AU 752800 B2 20021003

EP 1011690 A1 20000628 EP 1998-933196 19980701

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI

JP 2002509538 T2 20020326 JP 1999-507459 19980701

NZ 502134 A 20020328 NZ 1998-502134 19980701

PRIORITY APPLN. INFO.:

US 1997-887994 A 19970703

WO 1998-US13997 W 19980701

AB A carrier and a method for prepg. it are provided for use in the delivery of therapeutic agents. A polysaccharide is reacted with an oxidizing agent to open sugar rings on the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent oxime linkages with a second polysaccharide and each of the first and second polysaccharide is selected from the group consisting of hyaluronic acid, dextran, dextran sulfate, chondroitin sulfate, dermatan sulfate, keratan sulfate, heparan, heparan sulfate and alginate. Hyaluronic acid was treated with ethylenediamine and EDC to give a deriv., which was mixed with an oxidized hyaluronic acid to form a gel. BFGF was incorporated into the above gel.

IC ICM A61K031-715

ICS A61K009-14

CC 63-6 (Pharmaceuticals)

IT **Bone formation**

(crosslinked polysaccharide drug carriers)

IT Cytokines

DNA

**Growth factors, animal**

Hormones, animal, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(crosslinked polysaccharide drug carriers)

IT **9004-54-0D**, Dextran, derivs., crosslinked, biological studies

9005-32-7D, Alginic acid, derivs., crosslinked 9005-49-6D, Heparin, derivs., crosslinked, biological studies 9042-14-2D, Dextran sulfate, derivs., crosslinked 9050-30-0D, Heparan sulfate, derivs., crosslinked 9056-36-4D, Keratan sulfate, derivs., crosslinked 24967-94-0D, Dermatan sulfate, derivs., crosslinked **62031-54-3**, Fibroblast growth factor

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(crosslinked polysaccharide drug carriers)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 35 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:667970 HCAPLUS

DOCUMENT NUMBER: 129:301742

TITLE: Incorporation of amino acid analog(s) into polypeptides in proline auxotroph cells

INVENTOR(S): Gruskin, Elliott A.; Buechter, Douglas D.; Zhang, Guanghui; Connolly, Kevin

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 24 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent



LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                    | KIND | DATE     | APPLICATION NO. | DATE     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| US 5821089                                                                                                                                                                                                                                                                                                                    | A    | 19981013 | US 1996-655086  | 19960603 |
| CA 2328423                                                                                                                                                                                                                                                                                                                    | AA   | 19991125 | CA 1998-2328423 | 19980520 |
| WO 9960099                                                                                                                                                                                                                                                                                                                    | A1   | 19991125 | WO 1998-US10272 | 19980520 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG                                                                                                                                                        |      |          |                 |          |
| AU 9875813                                                                                                                                                                                                                                                                                                                    | A1   | 19991206 | AU 1998-75813   | 19980520 |
| AU 746967                                                                                                                                                                                                                                                                                                                     | B2   | 20020509 |                 |          |
| EP 1080182                                                                                                                                                                                                                                                                                                                    | A1   | 20010307 | EP 1998-923546  | 19980520 |
| R: CH, DE, ES, FR, GB, IT, LI, SE                                                                                                                                                                                                                                                                                             |      |          |                 |          |
| JP 2002515241                                                                                                                                                                                                                                                                                                                 | T2   | 20020528 | JP 2000-549707  | 19980520 |
| US 6492508                                                                                                                                                                                                                                                                                                                    | B1   | 20021210 | US 1998-169768  | 19981009 |
| PRIORITY APPLN. INFO.: US 1996-655086 A 19960603                                                                                                                                                                                                                                                                              |      |          |                 |          |
| WO 1998-US10272 A 19980520                                                                                                                                                                                                                                                                                                    |      |          |                 |          |

AB Incorporation of certain amino acid analogs into polypeptides produced by cells which do not ordinarily provide polypeptides contg. such amino acid analogs is accomplished by subjecting the cells to growth media contg. such amino acid analogs. The degree of incorporation can be regulated by adjusting the concn. of amino acid analogs in the media and/or by adjusting osmolality of the media. Such incorporation allows the chem. and phys. characteristics of polypeptides to be altered and studied. For example, hydroxyproline is incorporated into protein in Escherichia coli, Saccharomyces cerevisiae, or in a baculovirus expression system (Sf9 cells) under proline starvation conditions. Expression vectors contg. the gene for human type I (.alpha.1) collagen are transformed into prokaryotic or eukaryotic proline auxotrophs which depend upon externally supplied proline for protein synthesis and anabolism. Substitution of the amino acid analog(s) occurs since prolyl-tRNA is sufficiently promiscuous to allow misacylation of proline tRNA with the amino acid analog(s).

IC ICM C12P021-00  
 ICS C12N005-00

NCL 435071100

CC 16-4 (Fermentation and Bioindustrial Chemistry)

IT **Bone morphogenetic proteins**

RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)

(fusion protein with type I collagen .alpha.1 subunit; incorporation of amino acid analog(s) into polypeptides in proline auxotroph cells)

IT 50-99-7, Glucose, biological studies 56-40-6, Glycine, biological studies 57-50-1, Sucrose, biological studies 69-79-4, Maltose 7447-40-7, Potassium chloride (KCl), biological studies 7647-14-5, Sodium chloride, biological studies 7786-30-3, Magnesium chloride, biological studies 9004-34-6, Cellulose, biological studies 9004-54-0, Dextran, biological studies 25322-68-3  
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(osmolality increasing agent; incorporation of amino acid analog(s)  
into polypeptides in proline auxotroph cells)

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 36 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:635680 HCAPLUS

DOCUMENT NUMBER: 129:265493

TITLE: **Osteogenic** devices and methods of use  
thereof for repair of **bone**

INVENTOR(S): Rueger, David C.; Tucker, Marjorie M.; Chang, An-cheng

PATENT ASSIGNEE(S): Creative Biomolecules, Inc., USA

SOURCE: PCT Int. Appl., 147 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                | KIND | DATE     | APPLICATION NO. | DATE       |
|---------------------------------------------------------------------------|------|----------|-----------------|------------|
| WO 9841246                                                                | A2   | 19980924 | WO 1998-US6043  | 19980320   |
| WO 9841246                                                                | A3   | 19981022 |                 |            |
| W: AU, CA, JP                                                             |      |          |                 |            |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE    |      |          |                 |            |
| US 2001014662                                                             | A1   | 20010816 | US 1997-822186  | 19970320   |
| AU 9867795                                                                | A1   | 19981012 | AU 1998-67795   | 19980320   |
| AU 751451                                                                 | B2   | 20020815 |                 |            |
| EP 968012                                                                 | A2   | 20000105 | EP 1998-913183  | 19980320   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI |      |          |                 |            |
| JP 2001516262                                                             | T2   | 20010925 | JP 1998-540868  | 19980320   |
| PRIORITY APPLN. INFO.:                                                    |      |          | US 1997-822186  | A 19970320 |
|                                                                           |      |          | WO 1998-US6043  | W 19980320 |

AB Disclosed herein are improved **osteogenic** devices and methods of use thereof for repair of **bone** and cartilage defects. The devices and methods promote accelerated formation of repair tissue with enhanced stability using less **osteogenic** protein than devices in the art. Defects susceptible to repair with the instant invention include, but are not limited to crit. size defects, non-crit. size defects, non-union fractures, fractures, **osteochondral** defects, subchondral defects, and defects resulting from degenerative diseases such as **osteochondritis** dissecans.

IC ICM A61L027-00

CC 63-7 (Pharmaceuticals)

Section cross-reference(s): 2, 3

ST **bone** repair **osteogenic** protein sequence

IT **Bone morphogenetic proteins**

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(10; **osteogenic** devices and methods of use thereof for repair of **bone**)

IT **Bone morphogenetic proteins**

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(11; **osteogenic** devices and methods of use thereof for repair of **bone**)

- IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (12; **osteogenic** devices and methods of use thereof for repair of bone)
- IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (15; **osteogenic** devices and methods of use thereof for repair of bone)
- IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (16; **osteogenic** devices and methods of use thereof for repair of bone)
- IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (3; **osteogenic** devices and methods of use thereof for repair of bone)
- IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (5; **osteogenic** devices and methods of use thereof for repair of bone)
- IT Proteins, specific or class  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (60A; **osteogenic** devices and methods of use thereof for repair of bone)
- IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (6; **osteogenic** devices and methods of use thereof for repair of bone)
- IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (9; **osteogenic** devices and methods of use thereof for repair of bone)
- IT Proteins, specific or class  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (DPP (decapentaplegic); **osteogenic** devices and methods of use thereof for repair of bone)
- IT **Growth factors, animal**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (GDF1, growth differentiation factor 1; **osteogenic** devices and methods of use thereof for repair of bone)
- IT **Growth factors, animal**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (GDF10, growth differentiation factor 10; **osteogenic** devices and methods of use thereof for repair of bone)
- IT **Growth factors, animal**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU

(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (GDF11, growth differentiation factor 11; **osteogenic** devices  
 and methods of use thereof for repair of **bone**)

IT **Growth factors, animal**  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (GDF3, growth differentiation factor 3; **osteogenic** devices  
 and methods of use thereof for repair of **bone**)

IT **Growth factors, animal**  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (GDF6, growth differentiation factor 6; **osteogenic** devices  
 and methods of use thereof for repair of **bone**)

IT **Growth factors, animal**  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (GDF7, growth differentiation factor 7; **osteogenic** devices  
 and methods of use thereof for repair of **bone**)

IT **Growth factors, animal**  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (GDF8, growth differentiation factor 8; **osteogenic** devices  
 and methods of use thereof for repair of **bone**)

IT **Growth factors, animal**  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (GDF9, growth differentiation factor 9; **osteogenic** devices  
 and methods of use thereof for repair of **bone**)

IT Proteins, specific or class  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (OP-1; **osteogenic** devices and methods of use thereof for  
 repair of **bone**)

IT Proteins, specific or class  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (OP-2; **osteogenic** devices and methods of use thereof for  
 repair of **bone**)

IT Proteins, specific or class  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (OP-3; **osteogenic** devices and methods of use thereof for  
 repair of **bone**)

IT Proteins, specific or class  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (Vgl; **osteogenic** devices and methods of use thereof for  
 repair of **bone**)

IT Proteins, specific or class  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (Vgr; **osteogenic** devices and methods of use thereof for  
 repair of **bone**)

IT Cartilage  
 (formation of; **osteogenic** devices and methods of use thereof  
 for repair of **bone**)

IT Fibrins

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(glue; **osteogenic** devices and methods of use thereof for repair of **bone**)

## IT Binders

Physiological saline solutions  
Wetting agents

(**osteogenic** devices and methods of use thereof for repair of **bone**)

## IT Apatite-group minerals

Collagens, biological studies  
Fibrinogens  
Petrolatum

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(**osteogenic** devices and methods of use thereof for repair of **bone**)

## IT Proteins, specific or class

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(**osteogenic; osteogenic** devices and methods of use thereof for repair of **bone**)

IT **Bone formation**

(repair; **osteogenic** devices and methods of use thereof for repair of **bone**)

## IT Fats and Glyceridic oils, biological studies

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(sesame; **osteogenic** devices and methods of use thereof for repair of **bone**)

IT 69-65-8, Mannitol 1306-06-5, Hydroxyapatite 7758-87-4, Tricalcium phosphate 9002-04-4, Thrombin 9004-32-4, Sodium carboxymethylcellulose 9004-34-6D, Cellulose, alkyl derivs., biological studies **9004-54-0**, Dextran, biological studies 9004-62-0, Hydroxyethylcellulose 9004-65-3 9004-67-5, Methylcellulose 9032-42-2, Methylhydroxyethylcellulose

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(**osteogenic** devices and methods of use thereof for repair of **bone**)

L31 ANSWER 37 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:509084 HCAPLUS

DOCUMENT NUMBER: 129:140714

TITLE: Collagen-polysaccharide matrix for **bone** and cartilage repair

INVENTOR(S): Liu, Linshu; Spiro, Robert C.

PATENT ASSIGNEE(S): Orquest, Inc., USA

SOURCE: PCT Int. Appl., 37 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE  | APPLICATION NO. | DATE  |
|------------|------|-------|-----------------|-------|
| -----      | ---- | ----- | -----           | ----- |

WO 9831345 A1 19980723 WO 1998-US838 19980115  
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,  
 DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,  
 KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,  
 NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
 UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,  
 FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,  
 GA, GN, ML, MR, NE, SN, TD, TG  
 US 5866165 A 19990202 US 1997-783650 19970115  
 AU 9859203 A1 19980807 AU 1998-59203 19980115  
 AU 727430 B2 20001214  
 EP 994694 A1 20000426 EP 1998-902579 19980115  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI  
 JP 2000514698 T2 20001107 JP 1998-534551 19980115  
 JP 3348861 B2 20021120  
 NZ 336480 A 20010330 NZ 1998-336480 19980115

## PRIORITY APPLN. INFO.:

US 1997-783650 A 19970115  
 WO 1998-US838 W 19980115

- AB A matrix and a method for prepg. it are provided to support the growth of tissue, such as **bone**, cartilage or soft tissue. A polysaccharide is reacted with an oxidizing agent to open sugar rings on the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent linkages to collagen. Hyaluronic acid was treated with NaIO<sub>4</sub> to give hyaluronic polyaldehyde, which was mixed with collagens at the ratio of 1:1. The matrix was implanted into a defective area created in the parietal **bone** of rats. The radiog. anal. showed that all matrix-filled defects were completely radiodense, with no distinctive defect borders, which indicated complete healing.
- IC ICM A61K009-10  
 ICS A61K047-42; A61K047-36
- CC 63-7 (Pharmaceuticals)
- ST collagen polysaccharide matrix **bone** cartilage repair;  
 hyaluronate collagen matrix **bone** defect filler
- IT Musculoskeletal diseases  
 Musculoskeletal diseases  
 (cartilage, injury; collagen-polysaccharide matrix for **bone**  
 and cartilage repair)
- IT **Bone morphogenetic proteins**  
 Fibrinogens  
 Fibrins  
 Hedgehog protein  
 Interleukins  
**Platelet-derived growth factors**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (collagen-polysaccharide matrix for **bone** and cartilage  
 repair)
- IT **Growth factors, animal**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (differentiation factors; collagen-polysaccharide matrix for  
**bone** and cartilage repair)
- IT Cartilage  
 Cartilage  
 (disease, injury; collagen-polysaccharide matrix for **bone** and  
 cartilage repair)
- IT **Prosthetic materials and Prosthetics**

- (implants; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT **Bone, disease**  
**Bone, disease**  
 (injury; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Polysaccharides, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (oxidized, reaction products collagens; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Animal tissue  
 (soft, injury; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Collagens, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (type I, reaction products with oxidized polysaccharides; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT Collagens, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (type II, reaction products with oxidized polysaccharides; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT **Transforming growth factors**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (.beta.-; collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT 7790-28-5, Sodium periodate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (collagen-polysaccharide matrix for **bone** and cartilage repair)
- IT 9002-04-4, Thrombin **9004-54-0D**, Dextran, oxidized, reaction products with collagens, biological studies 9004-61-9D, Hyaluronic acid, oxidized, reaction products with collagens 9005-32-7D, Alginic acid, oxidized, reaction products with collagens 9007-28-7D, Chondroitin sulfate, oxidized, reaction products with collagens 9042-14-2D, Dextran sulfate, oxidized, reaction products with collagens 9050-30-0D, Heparan sulfate, oxidized, reaction products with collagens 9056-36-4D, Keratan sulfate, oxidized, reaction products with collagens 24967-94-0D, Dermatan sulfate, oxidized, reaction products with collagens **61912-98-9**, Insulin-like growth factor **62031-54-3**, Fibroblast growth factor 62683-29-8, Colony-stimulating factor 70226-44-7D, Heparan, oxidized, reaction products with collagens  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (collagen-polysaccharide matrix for **bone** and cartilage repair)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 38 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:479444 HCAPLUS

DOCUMENT NUMBER: 129:113542

TITLE: Functional group-containing plasma polymers as reactive coatings

INVENTOR(S): Chabrecek, Peter; Lohmann, Dieter

PATENT ASSIGNEE(S): Novartis A.-G., Switz.

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | KIND                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | DATE     | APPLICATION NO. | DATE       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|------------|
| WO 9828026                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | A1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 19980702 | WO 1997-EP7201  | 19971219   |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,<br>DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,<br>KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,<br>NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,<br>UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,<br>FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,<br>GA, GN, ML, MR, NE, SN, TD, TG |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |          |                 |            |
| AU 9859849                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | A1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 19980717 | AU 1998-59849   | 19971219   |
| AU 732216                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | B2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 20010412 |                 |            |
| EP 946220                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | A1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 19991006 | EP 1997-954745  | 19971219   |
| EP 946220                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | B1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 20030326 |                 |            |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,<br>IE, FI                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |          |                 |            |
| CN 1245439                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 20000223 | CN 1997-181530  | 19971219   |
| BR 9714429                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 20000425 | BR 1997-14429   | 19971219   |
| NZ 336158                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 20001222 | NZ 1997-336158  | 19971219   |
| JP 2001507255                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | T2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 20010605 | JP 1998-528383  | 19971219   |
| ZA 9711491                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 19980623 | ZA 1997-11491   | 19971222   |
| NO 9903064                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 19990621 | NO 1999-3064    | 19990621   |
| US 6436481                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | B1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 20020820 | US 1999-331516  | 19990622   |
| PRIORITY APPLN. INFO.:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |          | EP 1996-810890  | A 19961223 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |          | WO 1997-EP7201  | W 19971219 |
| AB                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | A substrate with a primary polymeric coating contg. reactive groups<br>predominantly on its surface is prepd. by plasma polymn. of an unsatd.<br>compd. contg. reactive groups onto the substrate, and the concn. of the<br>reactive groups in the coating, based on spin label detn. by ESR is 0.2-20<br>.times. 10 <sup>-9</sup> , and more preferably 2-12 .times. 10 <sup>-9</sup> . The reactive primary<br>coatings may be reacted with monomeric, oligomeric or macromol. compds. of<br>synthetic, semisynthetic or biol. origin to provide hybrid-type coated<br>articles (secondary coatings). Thus, a macromer of Fomblin ZDOL-KF 6001<br>(hydroxypropyl-terminated polydimethylsiloxane) triblock copolymer<br>functionalized with 2-isocyanatoethyl methacrylate was polymd. with TRIS<br>and N,N-dimethylacrylamide and molded to give contact lenses. The contact<br>lenses were then coated (grafted) by after-glow radio frequency plasma<br>polymn. of 2-isocyanatoethyl methacrylate onto the lenses. The concn. of<br>functional groups on the substrate surface was 4.09 .times. 10 <sup>-9</sup> . The<br>coated lenses were then treated with bovine serum albumin. The albumin<br>modified lens exhibited advancing angle 26, receding angel 19, and contact<br>angle hysteresis 7. |          |                 |            |
| IC                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | ICM A61L027-00                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |          |                 |            |
| CC                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | ICS A61L029-00; G02B001-04; C08J007-12                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |          |                 |            |
| IT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 63-6 (Pharmaceuticals)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |          |                 |            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Section cross-reference(s): 38, 42                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |          |                 |            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Artery                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |          |                 |            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Artery                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |          |                 |            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Bone                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |          |                 |            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Heart                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          |                 |            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Kidney                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |          |                 |            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Liver                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          |                 |            |



Organ, animal  
 Pancreas  
 Pancreas  
 (artificial; functional group-contg. plasma polymers as reactive coatings for medical goods)

IT Contact lenses  
**Dental materials and appliances**  
 Drug delivery systems  
 Intraocular lenses  
 Medical goods  
**Prosthetic materials and Prosthetics**  
**Prosthetic materials and Prosthetics**  
 (functional group-contg. plasma polymers as reactive coatings for medical goods)

IT **Prosthetic materials and Prosthetics**  
 (implants; functional group-contg. plasma polymers as reactive coatings for medical goods)

IT Agglutinins and Lectins  
 Antibodies  
 Antigens  
 Carbohydrates, biological studies  
 DNA  
 Enzymes, biological studies  
 Glycolipids  
 Glycopeptides  
 Glycoproteins, general, biological studies  
 Glycosaminoglycans, biological studies  
**Growth factors, animal**  
 Immunoglobulins  
 Lipoproteins  
 Nucleotides, biological studies  
 Oligosaccharides, biological studies  
 Peptides, biological studies  
 Phospholipids, biological studies  
 Polysaccharides, biological studies  
 RNA  
 Sphingolipids  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (reaction products with reactive coatings; functional group-contg. plasma polymers as reactive coatings for medical goods)

IT **9004-54-0D**, Dextran, reaction products with reactive coatings, biological studies 9005-49-6D, Heparin, reaction products with reactive coatings, biological studies 12619-70-4D, Cyclodextrin, reaction products with reactive coatings  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (functional group-contg. plasma polymers as reactive coatings for medical goods)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 39 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:544101 HCAPLUS

DOCUMENT NUMBER: 125:177462

TITLE: Surface-modified nanoparticles and method of making and using them

INVENTOR(S): Levy, Robert J.; Labhasetwar, Vinod; Song, Cunxian S.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 170 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

| PATENT NO.                                                                        | KIND | DATE     | APPLICATION NO. | DATE     |
|-----------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 9620698                                                                        | A2   | 19960711 | WO 1996-US476   | 19960104 |
| WO 9620698                                                                        | A3   | 19980122 |                 |          |
| W: AL, AM, AT, AU, CA, CH, CN, CZ, DE, DK, GB, HU, IS, JP, KE, LU, VN, MN, NO, US |      |          |                 |          |
| RW: KE, LS, SD, AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, PT, SE, NL, MR, NE, SN    |      |          |                 |          |
| CA 2207961                                                                        | AA   | 19960711 | CA 1996-2207961 | 19960104 |
| AU 9647556                                                                        | A1   | 19960724 | AU 1996-47556   | 19960104 |
| EP 805678                                                                         | A1   | 19971112 | EP 1996-903476  | 19960104 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE             |      |          |                 |          |
| JP 10511957                                                                       | T2   | 19981117 | JP 1996-521279  | 19960104 |
| PRIORITY APPLN. INFO.:                                                            |      |          | US 1995-369541  | 19950105 |
|                                                                                   |      |          | US 1995-389893  | 19950216 |
|                                                                                   |      |          | WO 1996-US476   | 19960104 |

AB Biodegradable controlled-release nanoparticles as sustained release bioactive agent delivery vehicles include surface modifying agents to target binding of the nanoparticles to tissues or cells of living systems, to enhance nanoparticle sustained release properties, and to protect nanoparticle-incorporated bioactive agents. Unique methods of making small (10 nm to 15 nm, and preferably 20 nm to 35 nm) nanoparticles having a narrow size distribution which can be surface-modified after the nanoparticles are formed is described. Techniques for modifying the surface include a lyophilization technique to produce a phys. adsorbed coating and epoxy-derivatization to functionalize the surface of the nanoparticles to covalently bind mols. of interest. The nanoparticles may also comprise hydroxy-terminated or epoxide-terminated and/or activated multiblock copolymers, having hydrophobic segments which may be polycaprolactone and hydrophilic segments. The nanoparticles are useful for local intravascular administration of smooth muscle inhibitors and antithrombogenic agents as part of interventional cardiac or vascular catheterization such as a balloon angioplasty procedure; direct application to tissues and/or cells for gene therapy, such as the delivery of **osteotropic** genes or gene segments into **bone** progenitor cells; or oral administration in an enteric capsule for delivery of protein/peptide based vaccines.

IC A61K009-51

CC 63-6 (Pharmaceuticals)

IT **Animal growth regulators**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (antagonists; surface-modified polymer controlled-release nanoparticles  
 for sustained drug delivery)

IT Albumins, biological studies  
 Alkaloids, biological studies  
 Antigens  
 Deoxyribonucleic acids  
 Enzymes  
 Gelatins, biological studies  
 Gene, animal

Glycoproteins, biological studies  
 Hormones  
 Nucleic acids  
     **Osteocalcins**  
 Phosphazene polymers  
 Phosphoproteins  
 Polyanhydrides  
 Polyesters, biological studies  
 Polyethers, biological studies  
 Quaternary ammonium compounds, biological studies  
 Ribonucleic acids  
 Toxins  
 Urethane polymers  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (surface-modified polymer controlled-release nanoparticles for  
     sustained drug delivery)

IT Sialoglycoproteins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (BSP II (**bone** sialoglycoprotein II), surface-modified polymer  
     controlled-release nanoparticles for sustained drug delivery)

IT **Dental materials and appliances**  
     (adhesives, surface-modified polymer controlled-release nanoparticles  
     for sustained drug delivery)

IT **Animal growth regulators**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (**blood platelet-derived growth**  
     **factors**, surface-modified polymer controlled-release  
     nanoparticles for sustained drug delivery)

IT Medical goods  
     (**bone** cements, surface-modified polymer controlled-release  
     nanoparticles for sustained drug delivery)

IT **Animal growth regulators**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (**bone morphogenetic proteins**,  
     surface-modified polymer controlled-release nanoparticles for sustained  
     drug delivery)

IT Glycophosphoproteins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (**osteonectins**, surface-modified polymer controlled-release  
     nanoparticles for sustained drug delivery)

IT Glycophosphoproteins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (**osteopontins**, surface-modified polymer controlled-release  
     nanoparticles for sustained drug delivery)

IT **Bone marrow**  
     (**osteoprogenitor** cell, surface-modified polymer  
     controlled-release nanoparticles for sustained drug delivery)

IT **Animal growth regulators**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (**transforming growth factors**,  
     surface-modified polymer controlled-release nanoparticles for sustained  
     drug delivery)

IT **62229-50-9**, Epidermal growth factor  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
     (heparin-binding, -like compds.; surface-modified polymer  
     controlled-release nanoparticles for sustained drug delivery)

IT 50-70-4, D-Glucitol, biological studies    57-09-0, Cetyl trimethyl

ammonium bromide 57-10-3, Hexadecanoic acid, biological studies  
 57-88-5, Cholesterol, biological studies 69-65-8, D-Mannitol 102-71-6,  
 Triethanolamine, biological studies 112-02-7, Hexadecyl trimethyl  
 ammonium chloride 151-21-3, Sodium dodecyl sulfate, biological studies  
 577-11-7, Sodium dioctyl sulfosuccinate 1069-55-2, Isobutyl  
 cyanoacrylate 3282-73-3, Didodecyldimethyl ammonium bromide 7445-62-7  
 7727-43-7, Barium sulfate 8007-43-0, Sorbitan sesquioleate 9000-65-1,  
 Tragacanth 9000-69-5, Pectin 9002-89-5, Polyvinyl alcohol 9002-92-0,  
 Polyoxyethylene lauryl ether 9003-39-8, Polyvinyl pyrrolidone  
 9003-53-6, Polystyrene 9004-32-4 9004-34-6, Cellulose, biological  
 studies 9004-35-7, Cellulose acetate 9004-44-8, Cellulose phthalate  
 9004-64-2, Hydroxypropyl cellulose 9004-99-3 9005-49-6, Heparin,  
 biological studies **9015-73-0** 9050-04-8, CM-cellulose calcium  
 9050-31-1, Hydroxypropyl methyl cellulose phthalate 10103-46-5, Calcium  
 phosphate 25322-68-3 106392-12-5, Poloxamer 110617-70-4, Poloxamine  
 128835-92-7, Lipofectin 180741-27-9

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(surface-modified polymer controlled-release nanoparticles for  
 sustained drug delivery)

IT 50-02-2, Dexamethasone 59-52-9 60-00-4, EDTA, biological studies  
 60-10-6, Dithizone 77-86-1 77-92-9, biological studies 87-69-4,  
 biological studies 92-84-2D, Phenothiazine, derivs. 102-71-6D,  
 Triethanolamine, fatty acid esters 139-13-9 144-62-7, Ethanedioic  
 acid, biological studies 1306-06-5, Hydroxyapatite 1338-39-2, Span 20  
 2462-63-7 9000-01-5, Acacia gum 9003-05-8, Polyacrylamide  
**9004-54-0**, Dextran, biological studies 9005-25-8, Starch,  
 biological studies 9005-32-7, Alginic acid 9012-76-4, Chitosan  
 10102-43-9D, Nitric oxide, compds. 11128-99-7, Angiotensin II  
 14930-96-2, Cytochalasin B **61912-98-9**, Insulin-like growth  
 factor 81845-44-5, Ciprostone 106096-92-8, Acidic fibroblast growth  
 factor 106096-93-9, Basic fibroblast growth factor 114949-22-3,  
 Activin 122647-31-8, Ibutilide 130736-65-1, U 86983

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(surface-modified polymer controlled-release nanoparticles for  
 sustained drug delivery)

L31 ANSWER 40 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:358762 HCAPLUS

DOCUMENT NUMBER: 122:170268

TITLE: Biocompatible implants carrying cells using a  
 retroviral expression vector for use in the  
 manufacture and secretion of therapeutic compounds

INVENTOR(S): Moullier, Philippe; Danos, Olivier; Heard,  
 Jean-Michel; Ferry, Nicolas

PATENT ASSIGNEE(S): Institut Pasteur, Fr.

SOURCE: PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.        | KIND | DATE     | APPLICATION NO. | DATE     |
|-------------------|------|----------|-----------------|----------|
| WO 9424298        | A1   | 19941027 | WO 1994-FR456   | 19940421 |
| W: AU, CA, JP, US |      |          |                 |          |

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
 FR 2704236 A1 19941028 FR 1993-4700 19930421  
 FR 2704236 B1 19950623  
 FR 2708202 A1 19950203 FR 1993-9185 19930726  
 FR 2708202 B1 19960329  
 AU 9466812 A1 19941108 AU 1994-66812 19940421  
 AU 688321 B2 19980312  
 EP 702723 A1 19960327 EP 1994-914431 19940421  
 EP 702723 B1 20020904  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE  
 JP 08508880 T2 19960924 JP 1994-522856 19940421  
 EP 1231277 A2 20020814 EP 2002-3797 19940421  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE  
 AT 223493 E 20020915 AT 1994-914431 19940421  
 ES 2181717 T3 20030301 ES 1994-914431 19940421  
 US 5906817 A 19990525 US 1996-532814 19960119  
 AU 9859675 A1 19980604 AU 1998-59675 19980330  
 AU 704371 B2 19990422  
 US 6326195 B1 20011204 US 1999-225509 19990106  
 US 2002098223 A1 20020725 US 2001-987601 20011115

## PRIORITY APPLN. INFO.:

FR 1993-4700 A 19930421  
 FR 1993-9185 A 19930726  
 EP 1994-914431 A3 19940421  
 WO 1994-FR456 W 19940421  
 US 1996-532814 A3 19960119  
 US 1999-225509 A3 19990106

- AB Neo-organ implants for use preferably in the peritoneal cavity of the recipient are described for use in the in situ synthesis and secretion of a therapeutic compd. The implant includes a biocompatible support for anchoring of cells that can secrete a therapeutic compd. embedded in a collagen gel. The cells may naturally synthesize the compd. or they may be transformed with a novel retrovirus expression vector from which the gag, pol, and env genes have been deleted to prevent viral replication. Fibroblasts transformed with a Moloney murine leukemia virus-based expression vector (M48) carrying .beta.-glucuronidase gene under control of the PGK promoter were immobilized on collagen-coated PTFE fibers and incorporated into a collagen gel in the presence of basic fibroblast growth factor. The implant was then introduced into the peritoneal cavity by attachment to the arms of the intestine in contact with the mesentery; the implant did not give rise to an inflammatory response. In animals showing a genetic .beta.-glucuronidase deficiency the implants caused a rapid fall in urinary secretion of intermediates from the catabolism of mucopolysaccharides and a spectacular normalization of the histol. of the liver and spleen.
- IC ICM C12N015-86  
 ICS A61K048-00; C12N005-10; A61L027-00; A61K009-14; C12N009-24; C12N015-27; C12N009-12; C12N015-12; C12N015-56; C12N015-54
- CC 63-7 (Pharmaceuticals)
- IT **Bone**  
 (powd., as substrate for immobilization of cells for implants; biocompatible implants carrying cells using a retroviral expression vector for use in the manuf. and secretion of therapeutic compds.)
- IT **Animal growth regulators**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (angiogenic factors, as angiogenic factor in implants contg. transgenic cells; biocompatible implants carrying cells using a retroviral expression vector for use in the manuf. and secretion of therapeutic

compsd.)

**IT Prosthetic materials and Prosthetics**

(implants, biocompatible implants carrying cells using a retroviral expression vector for use in the manuf. and secretion of therapeutic compds.)

IT 9002-84-0, PTFE **9004-54-0**, Dextran, biological studies  
9004-61-9, Hyaluronic acid

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(as substrate for immobilization of cells for implants; biocompatible implants carrying cells using a retroviral expression vector for use in the manuf. and secretion of therapeutic compds.)

L31 ANSWER 41 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:253359 HCAPLUS

DOCUMENT NUMBER: 120:253359

TITLE: Biocompatible polymer conjugates of natural polymers

INVENTOR(S): Rhee, Woonza; Wallace, Donald G.; Michaels, Alan S.;  
Burns, Ramon A., Jr.; Fries, Louis; Delustro, Frank;  
Bentz, Hanne; Mccullough, Kimberly; Damani, Ramesh;  
Berg, Richard A.

PATENT ASSIGNEE(S): Collagen Corp., USA

SOURCE: PCT Int. Appl., 103 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

| PATENT NO.                                                            | KIND | DATE     | APPLICATION NO. | DATE        |
|-----------------------------------------------------------------------|------|----------|-----------------|-------------|
| WO 9401483                                                            | A1   | 19940120 | WO 1993-US6292  | 19930701    |
| W: AU, JP                                                             |      |          |                 |             |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE    |      |          |                 |             |
| US 5324775                                                            | A    | 19940628 | US 1992-907518  | 19920702    |
| US 5328955                                                            | A    | 19940712 | US 1992-922541  | 19920730    |
| US 5292802                                                            | A    | 19940308 | US 1992-985680  | 19921202    |
| US 5308889                                                            | A    | 19940503 | US 1992-984197  | 19921202    |
| AU 9346620                                                            | A1   | 19940131 | AU 1993-46620   | 19930701    |
| AU 677789                                                             | B2   | 19970508 |                 |             |
| EP 648239                                                             | A1   | 19950419 | EP 1993-916926  | 19930701    |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE |      |          |                 |             |
| JP 08502082                                                           | T2   | 19960305 | JP 1993-503427  | 19930701    |
| PRIORITY APPLN. INFO.:                                                |      |          | US 1992-907518  | A 19920702  |
|                                                                       |      |          | US 1992-922541  | A 19920730  |
|                                                                       |      |          | US 1992-984197  | A 19921202  |
|                                                                       |      |          | US 1992-984933  | A 19921202  |
|                                                                       |      |          | US 1992-985680  | A 19921202  |
|                                                                       |      |          | US 1993-25032   | A 19930302  |
|                                                                       |      |          | US 1988-274071  | B2 19881121 |
|                                                                       |      |          | US 1989-433441  | A2 19891114 |
|                                                                       |      |          | WO 1993-US6292  | A 19930701  |

AB Non-immunogenic conjugates are formed by covalently binding a biol. inactive, natural polymer or deriv. thereof to synthetic hydrophilic polymers, e.g. PEG, via specific types of chem. bonds. The biocompatible conjugates can be used for soft tissue augmentation and for coating or forming various articles. The compns. may include other components such as liq., pharmaceutically acceptable carriers to form injectable

formulations, and/or biol. active proteins such as growth factors or cytokines. A soln. of transforming growth factor .beta.1 (TGF-.beta.1) was added to a soln. of difunctionally activated PEG and the mixt. was allowed to react for 2 min at 17.degree.. To this soln. was added a fibrillar atelopeptide collagen soln. and the resulting mixt. allowed to incubate overnight at ambient temp. to form pellets comprising collagen-PEG-TGF-.beta.1 conjugate. After washing the pellets 6 times with phosphate buffer .apprx.50% of TGF-.beta.1 was retained in the compn.

- IC ICM C08G063-48
- ICS C08G063-91; C08H001-00; A61K037-12
- CC 63-5 (Pharmaceuticals)
- Section cross-reference(s): 38
- IT Gelatins, biological studies
- Rubber, silicone, biological studies
- RL: BIOL (Biological study)
- (beads, pharmaceutical compn. contg. conjugates of natural and synthetic polymers and, for repair of **bone** defects)
- IT **Animal growth regulators**
- Glycosaminoglycans, biological studies
- Interferons
- Lymphokines and Cytokines
- RL: BIOL (Biological study)
- (conjugates with synthetic polymers, pharmaceutical compn. contg.)
- IT Glass, oxide
- RL: BIOL (Biological study)
- (beads, pharmaceutical compn. contg. conjugates of natural and synthetic polymers and, for repair of **bone** defects)
- IT **Animal growth regulators**
- RL: BIOL (Biological study)
- (**blood platelet-derived growth factors, AA**, conjugates with synthetic polymers, pharmaceutical compn. contg.)
- IT **Animal growth regulators**
- RL: BIOL (Biological study)
- (**blood platelet-derived growth factors, AB**, conjugates with synthetic polymers, pharmaceutical compn. contg.)
- IT **Animal growth regulators**
- RL: BIOL (Biological study)
- (**blood platelet-derived growth factors, BB**, conjugates with synthetic polymers, pharmaceutical compn. contg.)
- IT **Animal growth regulators**
- RL: BIOL (Biological study)
- (**bone morphogenetic proteins**, conjugates with synthetic polymers, pharmaceutical compn. contg.)
- IT Gels
- (hydro-, beads, pharmaceutical compn. contg. conjugates of natural and synthetic polymers and, for repair of **bone** defects)
- IT **Animal growth regulators**
- RL: BIOL (Biological study)
- (**osteogenins**, conjugates with synthetic polymers, pharmaceutical compn. contg.)
- IT **Animal growth regulators**
- RL: BIOL (Biological study)
- (**.beta.-transforming growth factors**, conjugates with synthetic and natural polymers,

pharmaceutical compn. contg.)

IT **Animal growth regulators**  
 RL: BIOL (Biological study)  
 (.beta.2-transforming growth factors, conjugates with synthetic and natural polymers, pharmaceutical compn. contg.)

IT 409-21-2, Silicon carbide, biological studies 1306-06-5, Hydroxyapatite 7758-87-4, Tricalcium phosphate 9002-84-0, Ptfе  
 RL: BIOL (Biological study)  
 (beads, pharmaceutical compn. contg. conjugates of natural and synthetic polymers and, for repair of bone defects)

IT **62229-50-9**, Epidermal growth factor  
 RL: BIOL (Biological study)  
 (conjugates with synthetic polymers, pharmaceutical compn. contg.)

IT 9004-34-6D, Cellulose, ethers, conjugates with synthetic polymers  
**9004-54-0D**, Dextran, conjugates with synthetic polymers  
 9004-61-9D, Hyaluronic acid, conjugates with synthetic polymers  
 9004-62-0D, Hydroxyethyl cellulose, conjugates with synthetic polymers  
 9005-25-8D, Starch, conjugates with synthetic polymers 9061-61-4D, Nerve growth factor, conjugates with synthetic and natural polymers  
 11096-26-7D, Erythropoietin, conjugates with synthetic and natural polymers 12619-70-4D, Cyclodextrin, conjugates with synthetic polymers  
 24967-93-9D, Chondroitin sulfate a, conjugates with synthetic polymers  
 24967-94-0D, Dermatan sulfate, conjugates with synthetic polymers  
 25322-46-7D, Chondroitin sulfate c, conjugates with synthetic polymers  
**61912-98-9D**, Insulin-like growth factor, conjugates with synthetic and natural polymers 62683-29-8D, Colony stimulating factor, conjugates with synthetic and natural polymers 69344-76-9D, Connective tissue-activating peptide I, conjugates with synthetic and natural polymers 106096-92-8D, Acidic fibroblast growth factor, conjugates with synthetic and natural polymers 106096-93-9D, Basic fibroblast growth factor, conjugates with synthetic and natural polymers 111575-54-3D, conjugates with collagen 154467-38-6D, conjugates with collagen 154467-39-7  
 RL: BIOL (Biological study)  
 (pharmaceutical compn. contg.)

L31 ANSWER 42 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1992:91479 HCAPLUS

DOCUMENT NUMBER: 116:91479

TITLE: Surgical implant and method incorporating chemotherapeutic agents

INVENTOR(S): Jernberg, Gary R.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND                                                                                                           | DATE     | APPLICATION NO. | DATE     |
|------------|----------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 9117744 | A1                                                                                                             | 19911128 | WO 1991-US2784  | 19910423 |
| W:         | AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU |          |                 |          |
| RW:        | AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT,                                                |          |                 |          |



LU, ML, MR, NL, SE, SN, TD, TG

|            |    |          |                 |          |
|------------|----|----------|-----------------|----------|
| CA 2082398 | AA | 19911115 | CA 1991-2082398 | 19910423 |
| AU 9179096 | A1 | 19911210 | AU 1991-79096   | 19910423 |
| EP 528971  | A1 | 19930303 | EP 1991-910569  | 19910423 |
| EP 528971  | B1 | 19990901 |                 |          |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

US 5290271 A 19940301 US 1993-99265 19930729

PRIORITY APPLN. INFO.: US 1990-523067 19900514

US 1990-599699 19901018

WO 1991-US2784 19910423

US 1992-899096 19920615

AB A surgical implant which provides controlled release and improved cellular uptake of chemotherapeutic agents over a predetd. period of time, is prepd. by incorporating time-release microshapes encapsulating .gtoreq.1 chemotherapeutic agent and carrier agents into a biocompatible implant. The implant can be a vascular graft, heart valve leaflet, artificial skin, etc.

IC ICM A61K009-22

ICS A61K009-52; A61L027-00

CC 63-7 (Pharmaceuticals)

IT **Animal growth regulators**

RL: BIOL (Biological study)

(bone morphogenetic protein, surgical implants contg. microencapsulated)

IT **Prosthetic materials and Prosthetics**

(implants, microencapsulated chemotherapeutics in)

IT **Prosthetic materials and Prosthetics**

(implants, vascular, microencapsulated chemotherapeutics in)

IT 50-02-2, Dexamethasone 50-23-7, Hydrocortisone 50-24-8, Prednisolone 53-06-5, Cortisone 53-86-1, Indomethacin 60-54-8, Tetracycline 114-07-8, Erythromycin 378-44-9, .beta.-Methasone 443-48-1, Metronidazole 644-62-2, Meclofenamic acid 1404-04-2, Neomycin 1404-90-6, Vancomycin 1406-05-9, Penicillin 5104-49-4 8063-07-8, Kanamycin 9004-54-0, Dextran, biological studies 9005-49-6, Heparin, biological studies 11111-12-9, Cephalosporin 15687-27-1, Ibuprofen 22204-53-1, Naproxen 35121-78-9, Prostacyclin

RL: BIOL (Biological study)

(surgical implants contg. microencapsulated)

L31 ANSWER 43 OF 43 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1990:538563 HCAPLUS

DOCUMENT NUMBER: 113:138563

TITLE: Purified particulate **bone** mineral for prosthetic **bone** replacement

INVENTOR(S): Pfirrmann, Rolf Wilhelm

PATENT ASSIGNEE(S): Geistlich, Ed, Sohne A.-G. fuer Chemische Industrie, Switz.; Holmes, Michael John

SOURCE: PCT Int. Appl., 16 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|------------|------|----------|-----------------|----------|
| -----      | ---- | -----    | -----           | -----    |
| WO 9001955 | A1   | 19900308 | WO 1989-GB1020  | 19890816 |

W: CH, DE, GB, JP, US  
 RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE  
 JP 04501070 T2 19920227 JP 1989-509992 19890816  
 EP 489728 A1 19920617 EP 1989-910649 19890816  
 EP 489728 B1 19970129  
 R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE  
 AT 148350 E 19970215 AT 1989-910649 19890816  
 CA 1336402 A1 19950725 CA 1989-608699 19890818  
 US 5573771 A 19961112 US 1995-391247 19950221  
 PRIORITY APPLN. INFO.: GB 1988-19755 19880819  
 WO 1989-GB1020 19890816  
 US 1990-469609 19900619  
 US 1992-876114 19920429  
 US 1993-115792 19930903  
 US 1994-258361 19940610

OTHER SOURCE(S): MARPAT 113:138563

AB A purified particulate **bone** mineral product comprises mineral particles free from all endogenous org. material and has resorbable, physiol. compatible, natural or synthetic macromol. material at the surface. The product is used as remodelling implants or prosthetic **bone** replacement. Aq. formaldehyde was added to 60.degree. gelatin soln. and deproteinated bovine femur cancellous **bone** pieces were added to the mixt. and vacuum applied and released for five times. The mixt. was left to stand at room temp. for 7 days and the **bone** pieces were then sepd. from the gel and dried in vacuum. The treated **bone** pieces were packed in polyethylene containers and sterilized by .gamma.-irradn. The ball pressure hardness and compressive strength was 5.1 and 4, compared to 2.5 and 0.8 N/mm2, resp. for the control without gelatin coating.

IC ICM A61L027-00  
 CC 63-7 (Pharmaceuticals)  
 ST **bone** mineral particulate gelatin coating; prosthetic implant  
**bone** mineral macromol matrix  
 IT Collagens, biological studies  
 Gelatins, biological studies  
 RL: BIOL (Biological study)  
 (**bone** mineral particulate coated with, for implant)  
 IT **Animal growth regulators**  
 RL: BIOL (Biological study)  
 (**bone** mineral particulate contg., for implant)  
 IT **Animal growth regulators**  
 RL: BIOL (Biological study)  
 (angiogenic factors, **bone** mineral particulate contg., for implant)  
 IT **Bone**  
 (artificial, **bone** mineral particulate coated with macromols. as)  
 IT **Animal growth regulators**  
 RL: BIOL (Biological study)  
 (**bone morphogenetic protein, bone** mineral particulate contg., for implant)  
 IT **Bone**  
 (implant, **bone** mineral particulate coated with macromols. as)  
 IT **Prosthetic materials and Prosthetics**  
 (implants, **bone** mineral particulates coated with macromols. as, for **bone**)  
 IT Collagens, biological studies

- RL: BIOL (Biological study)  
(osseins, **bone** mineral particulate contg., for implant)
- IT **Animal growth regulators**  
RL: BIOL (Biological study)  
(**osteogenins**, **bone** mineral particulate contg., for implants)
- IT **Animal growth regulators**  
RL: BIOL (Biological study)  
(**transforming growth factors**, **bone** mineral particulate contg., for implant)
- IT **9004-54-0**, Dextran, biological studies  
RL: BIOL (Biological study)  
(**bone** mineral particulate coated with, for implant)
- IT 19388-87-5, Taurolidine 38668-01-8, Taurultam  
RL: BIOL (Biological study)  
(**bone** mineral particulate contg., for implants)

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|     |       |                         |        |                                                                                                |
|-----|-------|-------------------------|--------|------------------------------------------------------------------------------------------------|
| L7  | 13610 | SEA FILE=HCAPLUS ABB=ON | PLU=ON | DEXTRAN+NT/CT                                                                                  |
| L11 | 31790 | SEA FILE=HCAPLUS ABB=ON | PLU=ON | "GROWTH FACTORS, ANIMAL"+OLD/CT                                                                |
| L14 | 24623 | SEA FILE=HCAPLUS ABB=ON | PLU=ON | "PROSTHETIC MATERIALS AND PROSTHETICS"+OLD/CT                                                  |
| L15 | 4540  | SEA FILE=HCAPLUS ABB=ON | PLU=ON | BONE FORMATION/CT                                                                              |
| L16 | 3800  | SEA FILE=HCAPLUS ABB=ON | PLU=ON | "BONE MORPHOGENETIC PROTEINS"+OLD,NT/CT                                                        |
| L17 | 20049 | SEA FILE=HCAPLUS ABB=ON | PLU=ON | "DENTAL MATERIALS AND APPLIANCES"+OLD/CT                                                       |
| L18 | 117   | SEA FILE=HCAPLUS ABB=ON | PLU=ON | "PROSTHETIC MATERIALS AND PROSTHETICS (L) MAXILLOFACIAL"/CT                                    |
| L24 | 17023 | SEA FILE=HCAPLUS ABB=ON | PLU=ON | EPIDERMAL GROWTH FACTOR/CT                                                                     |
| L25 | 18840 | SEA FILE=HCAPLUS ABB=ON | PLU=ON | "INSULIN-LIKE GROWTH FACTOR"+NT/CT                                                             |
| L26 | 3481  | SEA FILE=HCAPLUS ABB=ON | PLU=ON | "FIBROBLAST GROWTH FACTOR"/CT                                                                  |
| L27 | 21413 | SEA FILE=HCAPLUS ABB=ON | PLU=ON | "TRANSFORMING GROWTH FACTORS"+OLD,NT/CT                                                        |
| L28 | 8044  | SEA FILE=HCAPLUS ABB=ON | PLU=ON | "PLATELET-DERIVED GROWTH FACTORS"+OLD,NT/CT                                                    |
| L29 | 3800  | SEA FILE=HCAPLUS ABB=ON | PLU=ON | "BONE MORPHOGENETIC PROTEINS"+OLD,NT/CT                                                        |
| L30 | 51    | SEA FILE=HCAPLUS ABB=ON | PLU=ON | ((L24 OR L25 OR L26 OR L27 OR L28 OR L29) OR L11) AND L7 AND (L14 OR L15 OR L16 OR L17 OR L18) |
| L45 | 9     | SEA FILE=HCAPLUS ABB=ON | PLU=ON | L30 AND CROSSLINK?                                                                             |
| L47 | 6     | SEA FILE=HCAPLUS ABB=ON | PLU=ON | L30 AND (FREEZEDR? OR FREEZE DR?)                                                              |
| L49 | 1     | SEA FILE=HCAPLUS ABB=ON | PLU=ON | L47 AND HYDROGEL?                                                                              |
| L51 | 15    | SEA FILE=HCAPLUS ABB=ON | PLU=ON | L45 OR L47 OR L49                                                                              |

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L51 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2002:927491 HCAPLUS  
 DOCUMENT NUMBER: 138:8403  
 TITLE: **Crosslinked** elastin and process for producing the same  
 INVENTOR(S): Miyamoto, Keiichi  
 PATENT ASSIGNEE(S): Japan  
 SOURCE: PCT Int. Appl., 54 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                         | KIND | DATE     | APPLICATION NO. | DATE     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2002096978                                                                                                                                                                                      | A1   | 20021205 | WO 2002-JP5275  | 20020530 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, |      |          |                 |          |

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
 TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-163505 A 20010530

- AB Disclosed are **crosslinked** elastin; a water sol.  
**crosslinking** agent to be used in the **crosslinking**;  
 molded elastin articles; medical instruments and regeneration tissues  
 using the **crosslinked** elastin; and a surgical therapy and a  
 regeneration therapy with the use of these medical instruments. Thus, a  
 biocompatible functional material having an elasticity appropriate for  
 vital transplantation without causing release of cell-adhesive proteins is  
 provided.
- IC ICM C08H001-06  
 ICS C08L089-06; A61L027-22
- CC 63-7 (Pharmaceuticals)
- ST **crosslinked** elastin biocompatible prosthetic
- IT **Prosthetic materials and Prosthetics**  
 (implants; prosthetic materials and medical goods made of  
**crosslinked** elastins and functional substances)
- IT Medical goods  
 (prosthetic materials and medical goods made of **crosslinked**  
 elastins and functional substances)
- IT Caseins, biological studies  
 Ciliary neurotrophic factor  
 Collagens, biological studies  
 Elastins  
 Fibrins  
 Fibronectins  
 Fluoropolymers, biological studies  
 Gelatins, biological studies  
 Keratins  
 Laminins  
 Polyesters, biological studies  
 Polyoxyalkylenes, biological studies  
 Polysiloxanes, biological studies  
 Polyurethanes, biological studies  
 Sericins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (prosthetic materials and medical goods made of **crosslinked**  
 elastins and functional substances)
- IT Polysaccharides, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (soy; prosthetic materials and medical goods made of  
**crosslinked** elastins and functional substances)
- IT **Transforming growth factors**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (.alpha.-; prosthetic materials and medical goods made of  
**crosslinked** elastins and functional substances)
- IT 821-38-5, 1,12-Dodecanedicarboxylic acid 32279-04-2,  
 4-Hydroxyphenyldimethylsulfonium methyl sulfate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prosthetic materials and medical goods made of **crosslinked**  
 elastins and functional substances)

IT 476628-71-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (prosthetic materials and medical goods made of **crosslinked**  
 elastins and functional substances)

IT 1398-61-4, Chitin 9000-01-5, Arabic gum 9000-07-1, Carrageenan  
 9000-36-6, Karaya gum 9000-65-1, Traganth gum 9002-04-4, Thrombin  
 9002-18-0, Agar 9002-84-0, Polytetrafluoroethylene 9002-88-4,  
 Polyethylene 9002-89-5, Polyvinyl alcohol 9003-07-0, Polypropylene  
 9004-32-4, Sodium CMC 9004-34-6, Cellulose, biological studies  
**9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic  
 acid 9004-67-5, Methyl cellulose 9005-25-8, Starch, biological studies  
 9005-32-7, Alginic acid 9005-49-6, Heparin, biological studies  
 9007-27-6, Chondroitin 9007-28-7, Chondroitin sulfate 9011-14-7,  
 Poly(methyl methacrylate) 9012-76-4, Chitosan 9016-00-6,  
 Polydimethylsiloxane 9032-43-3, Cellulose sulfate 9042-14-2, Dextran  
 sulfate 9057-02-7, Pullulan 11078-30-1, Galactomannan 11078-31-2,  
 Glucomannan 11138-66-2, Xanthan gum 24967-94-0, Dermatan sulfate  
 24980-41-4, Polycaprolactone 24991-23-9 25038-59-9, Polyethylene  
 terephthalate, biological studies 25104-18-1, Polylysine 25190-06-1,  
 Polytetramethylene glycol 25248-42-4, Polycaprolactone 25249-06-3,  
 Polygalacturonic acid 25322-68-3, Polyethylene glycol 25322-69-4,  
 Polypropylene glycol 25513-46-6, Polyglutamic acid 26023-30-3,  
 Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid  
 31900-57-9, Dimethylsilanediol homopolymer 37294-28-3, Xyloglucan  
 37339-90-5, Lentinan 38000-06-5, Polylysine 52519-63-8, Carboxymethyl  
 chitin 54724-00-4, Curdlan **62229-50-9**, Epidermal growth factor  
 71010-52-1, Gellan gum 71010-52-1D, Gellan gum, sulfated 78644-42-5,  
 Polymalic acid 78666-19-0, Polymalic acid sru 106096-93-9, Basic FGF  
 127464-60-2, Vascular endothelial growth factor  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (prosthetic materials and medical goods made of **crosslinked**  
 elastins and functional substances)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:482991 HCAPLUS

DOCUMENT NUMBER: 137:52468

TITLE: **Crosslinkable** macromers for preparation of  
 matrixes for implanted articles

INVENTOR(S): Chudzik, Stephen J.; Clapper, David L.

PATENT ASSIGNEE(S): Surmodics, Inc., USA

SOURCE: U.S., 14 pp., Cont.-in-part of U. S. 6,156,345.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| US 6410044    | B1   | 20020625 | US 2000-571525  | 20000516 |
| US 6007833    | A    | 19991228 | US 1998-121248  | 19980723 |
| US 6156345    | A    | 20001205 | US 1999-469976  | 19991221 |
| WO 2002100453 | A1   | 20021219 | WO 2001-US18345 | 20010607 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,  
 RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ,  
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2003031697 A1 20030213 US 2002-176203 20020620

PRIORITY APPLN. INFO.:

US 1998-78607P P 19980319

US 1998-121248 A3 19980723

US 1999-469976 A2 19991221

US 2000-571525 A1 20000516

AB A **crosslinkable** macromer system and related methods of prep. the system and using the system in the form of a **crosslinked** matrix between a tissue site and an implant article, such as a tissue implant or on the porous surface of a prosthetic device, is described. The macromer system includes two or more polymer-pendent polymerizable groups and one or more initiator groups (e.g., polymer-pendent initiator groups). The polymerizable groups and the initiator group(s), when polymer-pendent, can be pendent on the same or different polymeric backbones. The macromer system provides advantages over the use of polymerizable macromers and sep., low mol. wt. initiators, including advantages with respect to such properties as nontoxicity, efficiency, and soly. A macromer system of the invention can be used as an interface between the tissue site and implant article in a manner sufficient to permit tissue growth through the **crosslinked** matrix and between the tissue site and implant. In a preferred embodiment, polymers with pendent polymerizable groups, for use in the macromer system, are prep. by reacting a polysaccharide polymer with a reactive moiety in an org., polar solvent, such as formamide. For example, a biodegradable tissue adhesive was prep. contg. (i) 5% polymerizable hyaluronic acid, prep. by reaction of hyaluronic acid and glycidyl acrylate in dry formamide, and (ii) 2% photoderivatized polyacrylamide, prep. from acrylamide and N-(3-aminopropyl)methacrylamide (APMA). The max. force generated by the adhesive prep. was 0.53 kg compared to 0.49 kg obtained for cyanoacrylate adhesive. Also, the photoderivatized polyacrylamide prep. was used in combination with polymerizable collagen (a reaction product of a mixt. of type I and type III collagen with acryloyl chloride) for prepn. of a scaffold contg. bone morphogenetic protein (BMP-7). The exptl. disks of solidified collagen scaffold contg. BMP-7 stimulated bone formation in a rat cranial onlay implant model.

IC ICM A61F002-06

ICS A61F002-28; A61F013-00; A61F047-30

NCL 424423000

CC 63-8 (Pharmaceuticals)

Section cross-reference(s): 35, 36

IT **Bone morphogenetic proteins**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(7; prepn. of **crosslinkable** macromers and polymer matrixes

for cell immobilization, tissue adherence and controlled drug delivery)

IT Peptides, biological studies

RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(active sites of biol. active proteins; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)

- IT Blood vessel  
Hip  
Joint, anatomical  
(artificial; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Adhesives  
(biol. tissue, biodegradable; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Drug delivery systems  
(controlled-release; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Medical goods  
(dressings; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT **Prosthetic materials and Prosthetics**  
(implants, vascular; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT **Dental materials and appliances**  
**Prosthetic materials and Prosthetics**  
(implants; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Joint, anatomical  
(knee, artificial; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Pore size  
Porosity  
(of implant surfaces; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Animal tissue  
Antibacterial agents  
Antimicrobial agents  
**Bone formation**  
**Crosslinking**  
Immobilization, molecular  
Polymerization catalysts  
Transplant and Transplantation  
Wound healing promoters  
(prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Vinyl compounds, uses  
RL: CAT (Catalyst use); USES (Uses)  
(prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Macromonomers  
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)



- IT Albumins, biological studies  
Collagens, biological studies  
Elastins  
Fibronectins  
Gelatin, biological studies  
Laminins  
Polysaccharides, biological studies  
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
(prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Eye  
(prostheses for; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Polymerization  
(radical; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Animal tissue  
(soft, prostheses; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Pentosans  
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
(sulfates; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Drug delivery systems  
(sustained-release, coatings for; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Medical goods  
(tissue adhesives, biodegradable; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Collagens, biological studies  
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
(type I; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Collagens, biological studies  
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
(type III; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT Hydrogels  
(wound dressings; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT 110-18-9, TEMED  
RL: NUU (Other use, unclassified); USES (Uses)  
(oxygen scavenger; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and

- controlled drug delivery)
- IT 9004-61-9DP, Hyaluronic acid, reaction products with glycidyl acrylate  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (polymerizable; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT 78-67-1, 2,2'-Azobisisobutyronitrile  
 RL: CAT (Catalyst use); USES (Uses)  
 (prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT 60-32-2, 6-Aminohexanoic acid 79-06-1, Acrylamide, reactions 80-62-6, Methyl methacrylate 88-12-0, reactions 95-96-5, 3,6-Dimethyl-1,4-dioxane-2,5-dione 106-90-1, Glycidyl acrylate 108-31-6, Maleic anhydride, reactions 502-44-3, .epsilon.-Caprolactone 814-68-6, Acryloyl chloride 6066-82-6, N-Hydroxysuccinimide 17372-87-1, Eosin Y 39148-58-8, 4-Benzoylbenzoyl chloride 42503-45-7, Pentaerythritol ethoxylate 51763-07-6, 7-Methyl-9-oxothioxanthene-3-carboxylic acid 72607-53-5, N-(3-Aminopropyl)methacrylamide hydrochloride 244211-74-3  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT 55750-53-3P, 6-Maleimidohexanoic acid 55750-63-5P 57079-14-8P 244202-40-2P 244202-41-3P 244202-49-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT 244202-45-7DP, acryloyl derivs. 244202-48-0P 244202-50-4P 244202-51-5P 438537-01-0P 438544-14-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT 9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid 9005-25-8, Starch, biological studies 9005-49-6, Heparin, biological studies 9007-28-7, Chondroitin sulfate 9012-76-4, Chitosan 9042-14-2, Dextran sulfate 9050-30-0, Heparan sulfate 9056-36-4, Keratan sulfate 24967-94-0, Dermatan sulfate  
 RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
 (prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT 106-90-1DP, Glycidyl acrylate, reaction products with hyaluronic acid 438537-00-9P  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT 56-81-5, Glycerol, biological studies 56-95-1, Chlorhexidine diacetate 102-71-6, Triethanolamine, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)
- IT 75-12-7, Formamide, uses  
 RL: NUU (Other use, unclassified); USES (Uses)

(solvent; prepn. of **crosslinkable** macromers and polymer matrixes for cell immobilization, tissue adherence and controlled drug delivery)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:353301 HCAPLUS

DOCUMENT NUMBER: 136:359642

TITLE: Mineralized collagen-polysaccharide matrix for bone and cartilage repair

INVENTOR(S): Liu, Lin Shu; Spiro, Robert C.

PATENT ASSIGNEE(S): Orquest, Inc., USA

SOURCE: PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | DATE     | APPLICATION NO. | DATE       |
|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|------------|
| WO 2002036147          | A1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 20020510 | WO 2001-US42477 | 20011005   |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |          |                 |            |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |          |                 |            |
| AU 2002011850          | A5                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 20020515 | AU 2002-11850   | 20011005   |
| PRIORITY APPLN. INFO.: |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          | US 2000-703438  | A 20001031 |
|                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          | WO 2001-US42477 | W 20011005 |
| AB                     | A matrix and a method for prepg. it are provided to support the growth of tissue, such as bone, cartilage or soft connective tissue. A polysaccharide is reacted with an oxidizing agent to open sugar rings on the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent linkages to mineralized collagen. The matrix can be implanted or injected, or the polyaldehyde polysaccharide and mineralized collagen starting minerals can be sep. injected to form the matrix in situ. Mineralized Type I collagen and polysaccharide-polyaldehyde were prepd. by mixing collagens with hyaluronate-polyaldehyde soln. Sodium cyanoborohydride was added to the mixt. to the final concn. of 10 mM. The resulting slurry was then poured into a mold and lyophilized. This formed a matrix, which was washed with water to remove NaCNBH3 and re-lyophilized. The surface property, structures and biol. activity of the matrixes were controlled by altering the ratio of the collagen to the polysaccharides, the type of polysaccharides, the d. of aldehyde groups generated on the polysaccharides, the d. of matrix, as well as the process of lyophilization. |          |                 |            |
| IC                     | ICM A61K038-16                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |          |                 |            |
| ICS                    | A61K038-17; A61K009-14; A61K035-14                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |          |                 |            |
| CC                     | 63-6 (Pharmaceuticals)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |          |                 |            |
| IT                     | <b>Growth factors, animal</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |          |                 |            |
| RL:                    | THU (Therapeutic use); BIOL (Biological study); USES (Uses)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |          |                 |            |

(ADMP 1; mineralized collagen-polysaccharide matrix for bone and cartilage repair)

IT **Prosthetic materials and Prosthetics**  
(implants; mineralized collagen-polysaccharide matrix for bone and cartilage repair)

IT Bone  
Cartilage  
Drying  
**Freeze drying**  
(mineralized collagen-polysaccharide matrix for bone and cartilage repair)

IT **Bone morphogenetic proteins**  
Fibrins  
**Growth factors, animal**  
Interleukins  
**Platelet-derived growth factors**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(mineralized collagen-polysaccharide matrix for bone and cartilage repair)

IT **Transforming growth factors**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.-; mineralized collagen-polysaccharide matrix for bone and cartilage repair)

IT **9004-54-ODP**, Dextran, reaction products with collagens  
9004-61-9DP, Hyaluronic acid, reaction products with collagens  
9005-32-7DP, Alginic acid, reaction products with collagens 9007-28-7DP,  
Chondroitin sulfate, reaction products with collagens 9042-14-2DP,  
Dextran sulfate, reaction products with collagens 9050-30-ODP, Heparan  
sulfate, reaction products with collagens 9056-36-4DP, Keratan sulfate,  
reaction products with collagens 24967-94-ODP, Dermatan sulfate,  
reaction products with collagens 70226-44-7DP, Heparan, reaction  
products with collagens  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); USES (Uses)  
(mineralized collagen-polysaccharide matrix for bone and cartilage  
repair)

IT **61912-98-9**, Insulin-like growth factor **62031-54-3**,  
Fibroblast growth factor 62683-29-8, CSF  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(mineralized collagen-polysaccharide matrix for bone and cartilage  
repair)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2001:792224 HCAPLUS  
DOCUMENT NUMBER: 135:335182  
TITLE: Collagen-polysaccharide matrix for treatment of bone  
tumors  
INVENTOR(S): Heidaran, Mohammad; Spiro, Robert C.  
PATENT ASSIGNEE(S): Orquest, Inc., USA  
SOURCE: U.S., 9 pp., Cont.-in-part of U.S. 5,972,385.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

| PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|------------|------|----------|-----------------|----------|
| US 6309670 | B1   | 20011030 | US 1999-324792  | 19990603 |
| US 5866165 | A    | 19990202 | US 1997-783650  | 19970115 |
| US 5972385 | A    | 19991026 | US 1998-7731    | 19980115 |

PRIORITY APPLN. INFO.: US 1997-783650 A2 19970115  
US 1998-7731 A2 19980115

AB A method of treatment for bone tumors comprising administering a matrix comprising collagen, a polysaccharide and a differentiation factor is provided. A polysaccharide is reacted with an oxidizing agent to open sugar rings on the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent linkages to collagen. For example, the collagen/hyaluronic acid/TGF-.beta. combination inhibited growth of the osteosarcoma cell line SK-ES-1 more potently than a combination of TGF-.beta. and collagen in a monolayer culture.

IC ICM A61K009-10  
ICS A61K047-42; A61K047-36

NCL 424486000

CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 2

IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(collagen-polysaccharide matrix contg. differentiation factors for treatment of bone tumors)

IT **Freeze drying**  
(prepn. of collagen-polysaccharide matrix contg. differentiation factors for treatment of bone tumors)

IT **Transforming growth factors**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.-; collagen-polysaccharide matrix contg. differentiation factors for treatment of bone tumors)

IT **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic acid 9005-32-7, Alginic acid 9007-28-7, Chondroitin sulfate 9042-14-2, Dextran sulfate 9050-30-0, Heparan sulfate 9056-36-4, Keratan sulfate 24967-94-0, Dermatan sulfate 70226-44-7, Heparan  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(collagen-polysaccharide matrix contg. differentiation factors for treatment of bone tumors)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2001:780648 HCAPLUS  
DOCUMENT NUMBER: 135:335147  
TITLE: Polymer-based injectable sustained release pharmaceutical compositions for peptide and protein drugs  
INVENTOR(S): Lee, Hee-yong; Lee, Hye-suk; Kim, Jung-soo; Kim, Sang-beom; Lee, Ji-suk; Choi, Ho-il; Chang, Seung-gu  
PATENT ASSIGNEE(S): Peptron Inc., S. Korea  
SOURCE: PCT Int. Appl., 37 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | KIND | DATE     | APPLICATION NO. | DATE       |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|------------|
| WO 2001078687                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | A1   | 20011025 | WO 2001-KR462   | 20010322   |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,<br>HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU,<br>LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,<br>SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,<br>ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,<br>DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,<br>BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG |      |          |                 |            |
| EP 1187602                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | A1   | 20020320 | EP 2001-917893  | 20010322   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,<br>IE, SI, LT, LV, FI, RO                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |      |          |                 |            |
| US 2003026844                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | A1   | 20030206 | US 2002-18870   | 20020418   |
| PRIORITY APPLN. INFO.:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |      |          |                 |            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |      |          | KR 2000-20484   | A 20000418 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |      |          | KR 2000-49344   | A 20000824 |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |      |          | WO 2001-KR462   | W 20010322 |

AB Controlled and sustained release injectable pharmaceutical compns. for a biopharmaceutical, such as peptides and proteins are described. Processes for prepn. of an injectable sustained release compn. comprises (i) a step of prepg. biodegradable porous microspheres having accessible ionic functional groups, (ii) a step of encapsulating a biopharmaceutical into the microspheres through ionic interaction by suspending or equilibrating the microspheres in a soln. contg. the biopharmaceutical, and (iii) a step of recovering and **freeze-drying** the biopharmaceutical-incorporated microspheres. For example, microspheres were prepd. by water/oil/water double emulsion solvent evapn. method using a hydrophilic 50:50 PLGA polymer (RG 502H), which contains free carboxy end groups. Deionized water (800 mL) was added to 1 g of PLGA polymer dissolved in 2 mL of methylene chloride and emulsified by sonication for 30 s using a probe type ultrasonic generator. This primary emulsion was dispersed into 200 mL of deionized water contg. 0.5% polyvinyl alc. (wt./vol.) in a vessel which connected to a const. temp. controller and mixed well by stirring for 15 min at 2500 rpm, 25.degree. using a mixer. After mixing for another 15 min at 1500 rpm, 25.degree., temp. of continuous phase was increased to 40.degree. to evap. methylene chloride. After 1 h stirring at 40.degree., 1500 rpm, temp. was decreased to 25.degree.. The hardened microspheres were collected by centrifugation and washed twice with 200 mL of deionized water, and then **freeze-dried**. The microspheres obtained were used for incorporation of protein drugs, i.e., ovalbumin, bovine serum albumin, human growth hormone, RNase A, or lysozyme through ionic interaction by simply soaking and equilibrating the microspheres into a buffer soln. having an appropriate concn. of protein.

IC ICM A61K009-22  
 CC 63-6 (Pharmaceuticals)  
 IT **Growth factors, animal**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (cartilage-inducing factor; prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs)

- IT **Growth factors, animal**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (osteogenic growth factors; prepn. of polymer-based injectable  
 sustained-release microspheres for peptide and protein drugs)
- IT Anti-infective agents  
 Antibacterial agents  
 Antiviral agents  
 Carboxyl group  
 Cryoprotectants  
 Evaporation  
 Fibrinolytics  
**Freeze drying**  
 Particle size  
 Phase separation  
 Pulmonary surfactant  
 Solvent extraction  
 (prepn. of polymer-based injectable sustained-release microspheres for  
 peptide and protein drugs)
- IT Annexins  
**Bone morphogenetic proteins**  
 Caseins, biological studies  
 Collagens, biological studies  
 Fibrinogens  
 Hemoglobins  
 Interferons  
 Interleukin 1  
 Interleukins  
 Lymphotoxin  
 Ovalbumin  
**Platelet-derived growth factors**  
 Polyanhydrides  
 Polycarbonates, biological studies  
 Polymer blends  
 Polysaccharides, biological studies  
 Proteins, general, biological studies  
 Transferrins  
**Transforming growth factors**  
 Tumor necrosis factors  
 Zeins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (prepn. of polymer-based injectable sustained-release microspheres for  
 peptide and protein drugs)
- IT 121-54-0, Benzethonium chloride 151-21-3, Sodium lauryl sulfate,  
 biological studies 577-11-7, Docusate sodium 1393-25-5, Secretin  
 1398-61-4, Chitin 1402-38-6, Oncostatin 8044-71-1, Cetrимide  
 9001-25-6, Blood-coagulation factor VII 9001-28-9, Factor IX  
 9001-63-2, Lysozyme 9002-01-1, Streptokinase 9002-60-2,  
 Adrenocorticotrophic hormone, biological studies 9002-61-3, Human  
 chorionic gonadotropin 9002-67-9, Luteinizing hormone 9002-68-0,  
 Follicle stimulating hormone 9002-69-1, Relaxin 9002-71-5, Thyroid  
 stimulating hormone 9002-72-6, Growth hormone 9002-89-5, Polyvinyl  
 alcohol 9004-10-8, Insulin, biological studies 9004-53-9, Dextrin  
**9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic  
 acid 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid  
 9005-49-6, Heparin, biological studies 9007-12-9, Calcitonin  
 9007-27-6, Chondroitin 9007-92-5, Glucagon, biological studies  
 9011-97-6, Cholecystokinin 9012-76-4, Chitosan 9015-71-8,

Corticotropin releasing factor 9034-39-3, Growth hormone releasing factor 9035-68-1, Proinsulin 9039-53-6, Urokinase 9041-92-3, .alpha.1-Antitrypsin 9054-89-1, Superoxide dismutase 9056-36-4, Keratan sulfate 9061-61-4, Nerve growth factor 11096-26-7, Erythropoietin 15802-18-3D, Cyanoacrylic acid, esters, polymers 24980-41-4, Polycaprolactone 25104-18-1, Poly(L-lysine) 25248-42-4, Polycaprolactone 25868-59-1 25931-47-9 26009-03-0, Polyglycolide 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26202-08-4, Polyglycolide 26680-10-4, Polylactide 26780-50-7, Poly(lactide-co-glycolide) 31621-87-1, Polydioxanone 34346-01-5, Resomer RG 502H 37221-79-7, Vasoactive intestinal polypeptide 38000-06-5, Poly(L-lysine) 52906-92-0, Motilin 57285-09-3, Inhibin 59392-49-3, Gastric inhibitory peptide 59763-91-6, Pancreatic polypeptide **61912-98-9**, Insulin-like growth factor **62229-50-9**, Epidermal growth factor 62683-29-8, Colony stimulating factor **67763-96-6**, Somatomedin C 77272-10-7, Macro cortin 80043-53-4, Gastrin releasing peptide 82657-92-9, Prourokinase 83652-28-2, Calcitonin gene-related peptide 85637-73-6, Atrial natriuretic factor 113189-02-9, Antihemophilic factor 139639-23-9, Tissue plasminogen activator

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of polymer-based injectable sustained-release microspheres for peptide and protein drugs)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:757812 HCAPLUS

DOCUMENT NUMBER: 135:308889

TITLE: **Crosslinked** polysaccharide drug carrier

INVENTOR(S): Spiro, Robert C.; Thompson, Andrea Y.; Liu, Linshu

PATENT ASSIGNEE(S): Orquest, Inc., USA

SOURCE: U.S., 7 pp., Cont.-in-part of U.S. Ser. No. 887,994, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE        |
|------------------------|------|----------|-----------------|-------------|
| US 6303585             | B1   | 20011016 | US 1998-110381  | 19980701    |
| US 2003012765          | A1   | 20030116 | US 2001-954855  | 20010917    |
| PRIORITY APPLN. INFO.: |      |          | US 1997-887994  | B2 19970703 |
|                        |      |          | US 1998-110381  | A1 19980701 |

AB A carrier and a method for prepg. it are provided for use in the delivery of therapeutic agents. A polysaccharide is reacted with an oxidizing agent to open sugar rings on the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent oxime linkages with a second polysaccharide and each of the first and second polysaccharide is selected from the group consisting of hyaluronic acid, dextran, dextran sulfate, chondroitin sulfate, dermatan sulfate, keratan sulfate, heparan, heparan sulfate and alginate. A hyaluronate amine deriv. was prepd. by treating hyaluronic acid with EDC and ethylenediamine.

IC ICM C08B037-00

ICS A61K031-715

NCL 514054000



CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 33

ST **crosslinked** polysaccharide drug carrier

IT Drug delivery systems  
 (carriers; **crosslinked** polysaccharide drug carrier)

IT **Bone formation**  
**Crosslinking**  
 Dissolution rate  
 (**crosslinked** polysaccharide drug carrier)

IT **Growth factors, animal**  
 Polysaccharides, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (**crosslinked** polysaccharide drug carrier)

IT 107-15-3DP, Ethylenediamine, reaction products with hyaluronic acid  
 9004-61-9DP, Hyaluronic acid, reaction products with ethylene diamine or  
 oxidized  
 RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (**crosslinked** polysaccharide drug carrier)

IT 106096-93-9, Basic fibroblast growth factor  
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (**crosslinked** polysaccharide drug carrier)

IT 9004-61-9, Hyaluronic acid  
 RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT  
 (Reactant or reagent); USES (Uses)  
 (**crosslinked** polysaccharide drug carrier)

IT **9004-54-0**, Dextran, biological studies 9005-32-7, Alginic acid  
 9005-49-6, Heparin, biological studies 9007-28-7, Chondroitin sulfate  
 9042-14-2, Dextran sulfate 9050-30-0, Heparan sulfate 9056-36-4,  
 Keratan sulfate 24967-94-0, Dermatan sulfate  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (**crosslinked** polysaccharide drug carrier)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:900497 HCAPLUS

DOCUMENT NUMBER: 134:61577

TITLE: Biologically active material based on an insolubilized  
 dextran derivative and a growth factor

INVENTOR(S): Blanchat, Cinderella; Logeart-avramoglou, Delphine;  
 Petite, Herve; Meunier, Alain; Chaubet, Frederic;  
 Jozefonvicz, Jacqueline; Jozefowicz, Marcel; Sedel,  
 Laurent; Correia, Jose

PATENT ASSIGNEE(S): Iterfi, Fr.

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2000076562 | A1   | 20001221 | WO 2000-FR1603  | 20000609 |
| W: CA, JP, US |      |          |                 |          |

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
PT, SE

FR 2794649 A1 20001215 FR 1999-7401 19990611  
FR 2794649 B1 20030411  
EP 1189644 A1 20020327 EP 2000-940481 20000609

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, FI

JP 2003501217 T2 20030114 JP 2001-502893 20000609  
US 2002169120 A1 20021114 US 2001-16706 20011211

PRIORITY APPLN. INFO.:

FR 1999-7401 A 19990611

WO 2000-FR1603 W 20000609

AB The invention concerns a biol. active material essentially comprising at least an insolubilized dextran deriv. of general formula DMCaBbSucSd and at least a growth factor having an activity on osteoarticular, dental and/or maxillofacial tissues, and the method for prep. same. The invention also concerns the uses of said biomaterial for prep. a repair or filling material, such as an implant, for osteoarticular, dental or maxillofacial applications and for prep. an orthopedic, dental or maxillofacial prosthesis, and the prosthesis coated with said biol. active material. A hydrogel comprising dextran derivs. **crosslinked** with sodium trimetaphosphate and 0.5 ng/gel bone morphogenic protein was prepd. and lyophilized to obtain a powder. Thus, 15 mg of the above powder was rehydrated with 100 .mu.L water and used as a bone implant to fill a bone cavity of about 50 mm<sup>3</sup>.

IC ICM A61L027-54

ICS A61L027-22; A61L027-20; A61L027-26; A61L027-48; A61L027-46

CC 63-7 (Pharmaceuticals)

IT **Bone formation**

Coral

**Crosslinking agents**

**Dental materials and appliances**

**Prosthetic materials and Prosthetics**

Tooth

(biol. active material based on insolubilized dextran deriv. and growth factor)

IT **Bone morphogenetic proteins**

**Growth factors, animal**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(biol. active material based on insolubilized dextran deriv. and growth factor)

IT **Prosthetic materials and Prosthetics**

(implants; biol. active material based on insolubilized dextran deriv. and growth factor)

IT **Prosthetic materials and Prosthetics**

(orthopedic; biol. active material based on insolubilized dextran deriv. and growth factor)

IT 1306-06-5, Hydroxyapatite 7758-87-4, Tricalcium phosphate

**9004-54-0D**, Dextran, derivs., biological studies 25322-68-3,

Polyethylene glycol 26009-03-0, Polyglycolic acid 26124-68-5,

Polyglycolic acid 34346-01-5, Glycolic acid lactic acid copolymer

RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(biol. active material based on insolubilized dextran deriv. and growth factor)

REFERENCE COUNT:

9

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS

## RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:627957 HCAPLUS

DOCUMENT NUMBER: 133:187992

TITLE: Positive-charged cross-linked polysaccharides for scar reduction

INVENTOR(S): Gruskin, Elliott A.; Christoforou, Christopher T.

PATENT ASSIGNEE(S): United States Surgical Corp., USA

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                        | KIND | DATE     | APPLICATION NO. | DATE        |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|-------------|
| WO 2000051566                                                                                                                                                                                                                                     | A1   | 20000908 | WO 2000-US5610  | 20000303    |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN |      |          |                 |             |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE                                                                                                                                                                        |      |          |                 |             |
| US 6410519                                                                                                                                                                                                                                        | B1   | 20020625 | US 2000-519006  | 20000303    |
| US 2003023209                                                                                                                                                                                                                                     | A1   | 20030130 | US 2002-58182   | 20020125    |
| PRIORITY APPLN. INFO.:                                                                                                                                                                                                                            |      |          | US 1999-122814P | P 19990304  |
|                                                                                                                                                                                                                                                   |      |          | US 2000-519006  | A1 20000303 |

AB A method of reducing scar formation at a wound site includes contacting the wound site with an effective scar reducing amt. of a cross-linked polysaccharide having a pos. charge and thereby reducing scar formation as the wound site heals. Such polysaccharide includes bioabsorbable cross-linked dextrans or alginates. The pos. charge may be provided by diethylaminoethyl (DEAE) moieties. The cross-linked polysaccharide can be applied to the wound site as a powder or bead. The cross-linked polysaccharide may also be contained in a compn. including a pharmaceutically acceptable vehicle. Biocompatible surgical devices are provided with an effective scar reducing amt. of a cross-linked polysaccharide having a pos. charge which reduce scar formation at healing wound sites. A method of reducing TGF-.beta. activity is also provided. Results of tests with DEAE-Sephadex beads are presented.

IC A61K009-14; A61K031-715; A61L017-10; A61L027-20

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

ST pos charged **crosslinked** polysaccharide scar wound; dextran pos charged **crosslinked** scar wound; alginate pos charged **crosslinked** scar wound; diethylaminoethyl **crosslinked** polysaccharide scar wound; surgical device pos charged **crosslinked** polysaccharide scar; Sephadex DEAE scar wound; TGFbeta modulation pos charged **crosslinked** polysaccharide

IT **Prosthetic materials and Prosthetics**

(implants; pos.-charged cross-linked polysaccharides for scar redn.)

IT **Transforming growth factors**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(.beta.-; pos.-charged cross-linked polysaccharides for scar redn.)

IT **9004-54-0D**, Dextran, pos.-charged cross-linked, biological studies  
 9064-92-0, DEAE-Sephadex  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pos.-charged cross-linked polysaccharides for scar redn.)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:513547 HCAPLUS

DOCUMENT NUMBER: 133:125280

TITLE: Compositions and methods for controlled delivery of virus vectors

INVENTOR(S): Levy, Robert J.; Jones, Peter L.

PATENT ASSIGNEE(S): Children's Hospital of Philadelphia, USA

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                                                        | KIND | DATE     | APPLICATION NO. | DATE     |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2000043044                                                                                                                                                                                                                                                                                                                                                     | A1   | 20000727 | WO 2000-US1193  | 20000119 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG                                                                                                                                                                                |      |          |                 |          |

PRIORITY APPLN. INFO.: US 1999-116405P P 19990119

AB The invention relates to compns. and methods for delivering a virus vector to an animal. The compns. include compns. which comprise a matrix having a virus vector bound at the exterior surface thereof in a physiol. reversible manner. The invention also includes methods of making such compns., including particles, devices, bulk materials, and other objects which comprise, consist of, or are coated with such compns. Methods of delivering a virus vector to an animal tissue are also described.

IC ICM A61K048-00

ICS C12N015-63; A61B019-00; C07H021-04

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 3

IT **Platelet-derived growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(-beta.; compns. and methods for controlled delivery of virus vectors)

IT **Bone morphogenetic proteins**

**Platelet-derived growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(compns. and methods for controlled delivery of virus vectors)

IT **Crosslinking agents**

(virus-binding; compns. and methods for controlled delivery of virus vectors)

IT **Transforming growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (.beta.-; compns. and methods for controlled delivery of virus vectors)

IT 9002-06-6, Thymidine kinase 9002-64-6, Pth 9002-72-6, Somatotropin 61912-98-9, Insulin like growth factor 62031-54-3, Fgf 139639-23-9, Tissue plasminogen activator

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (compns. and methods for controlled delivery of virus vectors)

IT 97-90-5, Ethylene glycol dimethacrylate 108-05-4D, Vinyl acetate, copolymers 1306-06-5, Hydroxyapatite 6606-65-1 7440-06-4, Platinum, biological studies 7440-32-6, Titanium, biological studies 7758-87-4, Tricalcium phosphate 9002-84-0, Polytetrafluoroethylene 9002-86-2, Polyvinyl chloride 9002-88-4, Polyethylene 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-07-0, Polypropylene 9003-17-2, Polybutadiene 9003-18-3 9003-20-7, Vinyl acetate homopolymer 9003-27-4, Polyisobutylene 9003-31-0, Polyisoprene 9003-39-8, Polyvinylpyrrolidone 9003-53-6, Polystyrene 9003-54-7, PolyStyrene acrylonitrile 9003-56-9 9004-35-7, Cellulose acetate 9004-53-9, Dextrin 9004-54-0, Dextran, biological studies 9005-32-7, Alginic acid 9011-14-7, Polymethylmethacrylate 9012-36-6, Agarose 9016-80-2, Polymethylpentene 9017-21-4, Polymethylstyrene 9046-31-5, Polystyrene carboxylic acid 10586-17-1, Isopropyl cyanoacrylate 12597-68-1, Stainless steel, biological studies 15802-18-3D, polyalkyl derivs. 21982-30-9, Hydroxymethyl methacrylate 24937-78-8, Ethylene vinyl acetate copolymer 24980-41-4, Polycaprolactone 24981-14-4, Polyvinyl fluoride 25014-41-9, Polyacrylonitrile 25068-26-2, Polymethylpentene 25087-26-7, Polymethacrylic acid 25102-52-7, Butadiene-isoprene copolymer 25248-42-4, Polycaprolactone 26009-03-0, Polyglycolic acid 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediy)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 34346-01-5, Glycolic acid-lactic acid copolymer 50851-57-5, Polystyrene sulfonic acid 61128-18-5, Caprolactone glycolic acid copolymer

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (controlled-delivery matrix; compns. and methods for controlled delivery of virus vectors)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:141482 HCAPLUS

DOCUMENT NUMBER: 132:185482

TITLE: Malleable paste for filling bone defects

INVENTOR(S): Gertzman, Arthur A.; Sunwoo, Moon Hae

PATENT ASSIGNEE(S): Musculoskeletal Transplant Foundation, USA

SOURCE: U.S., 7 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6  
PATENT INFORMATION:

| PATENT NO.                                                                                | KIND | DATE     | APPLICATION NO. | DATE     |
|-------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| US 6030635                                                                                | A    | 20000229 | US 1998-31750   | 19980227 |
| US 6326018                                                                                | B1   | 20011204 | US 1999-413815  | 19991007 |
| EP 1127581                                                                                | A1   | 20010829 | EP 2000-301370  | 20000222 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO |      |          |                 |          |
| US 6437018                                                                                | B1   | 20020820 | US 2000-515656  | 20000229 |
| US 6458375                                                                                | B1   | 20021001 | US 2000-677891  | 20001003 |

PRIORITY APPLN. INFO.:

|                |    |          |
|----------------|----|----------|
| US 1998-31750  | A3 | 19980227 |
| US 1999-365880 | B2 | 19990803 |
| US 2000-515656 | A2 | 20000229 |

AB The invention is directed toward a malleable bone putty and a flowable gel compn. for application to a bone defect site to promote new bone growth at the site which comprises a new bone growth inducing compd. of demineralized lyophilized allograft bone powder. The bone powder has a particle size ranging from about 100 to about 850 .mu. and is mixed in a high mol. wt. **hydrogel** carrier, the **hydrogel** component of the carrier ranging from 0.3 to 3.0% of the compn. and having a mol. wt. of about at least 10,000 Daltons. The compn. contains about 25% to about 40% bone powder and can be addnl. provided with BMP's and a sodium phosphate buffer. A malleable putty of 2% soln. hyaluronic acid in isotonic saline with 250-420 .mu. cortical allograft bone powder at 30%. **Freeze dried** cortical allograft bone (502 mg) of particle size ranging 250-420 .mu. was mixed into 1170 mg of a 2% soln. of sodium hyaluronate in isotonic saline. The bone component is added to achieve a bone concn. of 30% (wt./wt.). The soln. was well mixed and allowed to stand for 2-3 h at room temp. to provide a malleable putty with excellent formability properties.

IC ICM A61L025-00

ICS A61L015-64; A61K035-32

NCL 424423000

CC 63-7 (Pharmaceuticals)

IT Antibiotics

Antimicrobial agents

**Bone formation**

Particle size distribution

(malleable paste for filling bone defects)

IT **Bone morphogenetic proteins**

Enzymes, biological studies

Vitamins

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(malleable paste for filling bone defects)

IT 56-75-7, Chloromycetin 57-92-1, biological studies 60-54-8, Tetracycline 69-53-4, Ampicillin 114-07-8, Erythromycin 1306-06-5, Hydroxylapatite (Ca5(OH)(PO4)3) 1403-66-3, Gentamicin 1404-04-2, Neomycin 1404-26-8, Polymyxin B 1405-87-4, Bacitracin 1406-05-9, Penicillin 7440-70-2D, Calcium, salts, biological studies 7758-87-4, Calcium phosphate 7778-18-9 9001-12-1, Collagenase **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic acid 9012-76-4, Chitosan 9031-96-3, Peptidase 9035-73-8, Oxidase 9067-32-7, Sodium hyaluronate 10043-52-4, Calcium chloride (CaCl2), biological studies 18323-44-9, Clindamycin 25953-19-9, Cefazolin 32986-56-4 32988-50-4, Viomycin 104184-69-2, Azactam 106392-12-5, Pluronic 107043-88-9,

N,O-Carboxymethyl chitosan

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(malleable paste for filling bone defects)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:686567 HCAPLUS

DOCUMENT NUMBER: 131:303417

TITLE: Collagen-polysaccharide matrix for bone and cartilage repair

INVENTOR(S): Liu, Linshu; Spiro, Robert

PATENT ASSIGNEE(S): Orquest, Inc., USA

SOURCE: U.S., 10 pp., Cont.-in-part of U.S. 5,866,165.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE        |
|------------------------|------|----------|-----------------|-------------|
| US 5972385             | A    | 19991026 | US 1998-7731    | 19980115    |
| US 5866165             | A    | 19990202 | US 1997-783650  | 19970115    |
| US 6309670             | B1   | 20011030 | US 1999-324792  | 19990603    |
| PRIORITY APPLN. INFO.: |      |          | US 1997-783650  | A2 19970115 |
|                        |      |          | US 1998-7731    | A2 19980115 |

AB A matrix and a method for prepg. it are provided to support the growth of tissue, such as bone, cartilage or soft tissue. A polysaccharide is reacted with an oxidizing agent to open sugar rings on the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent linkages to collagen. Collagen-hyaluronate conjugates were prepd. according to above method suing sodium periodate. Above conjugate matrix was implanted into a 5 mm by 3 mm defect created in the parietal bone of rats. All matrix-filled defects were completely radiodense after 28 days, with no distinctive defect borders, which indicated complete healing. Unfilled defects appeased as ovoid radiolucent areas with rounded corners, suggesting minimal healing.

IC ICM A61K038-39

ICS A61K009-10; A61K047-42; A61K047-36

NCL 424486000

CC 63-7 (Pharmaceuticals)

IT **Freeze drying**

Freezing

(collagen-polysaccharide matrix for bone and cartilage repair)

IT **Bone morphogenetic proteins**

Interleukins

**Platelet-derived growth factors**

Proteins, general, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(collagen-polysaccharide matrix for bone and cartilage repair)

IT **Transforming growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.-; collagen-polysaccharide matrix for bone and cartilage repair)  
 IT **61912-98-9**, Insulin-like growth factor **62031-54-3**,  
 Fibroblast growth factor 62683-29-8, Colony-stimulating factor  
 173247-99-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(collagen-polysaccharide matrix for bone and cartilage repair)  
 IT **9004-54-ODP**, Dextran, conjugates with with collagen, biological studies 9004-61-9DP, Hyaluronic acid, conjugates with with collagen 9005-32-7DP, Alginic acid, conjugates with with collagen 9007-28-7DP, Chondroitin sulfate, conjugates with with collagen 9042-14-2DP, Dextran sulfate, conjugates with with collagen 9050-30-ODP, Heparan sulfate, conjugates with with collagen 9056-36-4DP, Keratan sulfate, conjugates with with collagen 70226-44-7DP, Heparan, conjugates with with collagen  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(collagen-polysaccharide matrix for bone and cartilage repair)  
 REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:48632 HCAPLUS

DOCUMENT NUMBER: 130:100691

TITLE: **Crosslinked** polysaccharide drug carrier

INVENTOR(S): Spiro, Robert C.; Thompson, Andrea Y.; Liu, Linshu

PATENT ASSIGNEE(S): Orquest, Inc., USA

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO.    | KIND                                                                                                                                                                                                                                                                                                                       | DATE     | APPLICATION NO. | DATE     |
|---------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 9901143    | A1                                                                                                                                                                                                                                                                                                                         | 19990114 | WO 1998-US13997 | 19980701 |
| W:            | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |          |
| RW:           | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG                                                                                                                                                         |          |                 |          |
| AU 9882909    | A1                                                                                                                                                                                                                                                                                                                         | 19990125 | AU 1998-82909   | 19980701 |
| AU 752800     | B2                                                                                                                                                                                                                                                                                                                         | 20021003 |                 |          |
| EP 1011690    | A1                                                                                                                                                                                                                                                                                                                         | 20000628 | EP 1998-933196  | 19980701 |
| R:            | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI                                                                                                                                                                                                                                                             |          |                 |          |
| JP 2002509538 | T2                                                                                                                                                                                                                                                                                                                         | 20020326 | JP 1999-507459  | 19980701 |
| NZ 502134     | A                                                                                                                                                                                                                                                                                                                          | 20020328 | NZ 1998-502134  | 19980701 |

PRIORITY APPLN. INFO.: US 1997-887994 A 19970703

WO 1998-US13997 W 19980701

AB A carrier and a method for prep. it are provided for use in the delivery of therapeutic agents. A polysaccharide is reacted with an oxidizing agent to open sugar rings on the polysaccharide to form aldehyde groups. The aldehyde groups are reacted to form covalent oxime linkages with a



second polysaccharide and each of the first and second polysaccharide is selected from the group consisting of hyaluronic acid, dextran, dextran sulfate, chondroitin sulfate, dermatan sulfate, keratan sulfate, heparan, heparan sulfate and alginate. Hyaluronic acid was treated with ethylenediamine and EDC to give a deriv., which was mixed with an oxidized hyaluronic acid to form a gel. BFGF was incorporated into the above gel.

IC ICM A61K031-715  
ICS A61K009-14

CC 63-6 (Pharmaceuticals)

ST **crosslinked** polysaccharide biodegradable carrier; hyaluronate **crosslinked** gel bFGF implant

IT Drug delivery systems  
(carriers; **crosslinked** polysaccharide drug carriers)

IT **Bone formation**  
(**crosslinked** polysaccharide drug carriers)

IT Polysaccharides, biological studies  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(**crosslinked** polysaccharide drug carriers)

IT Cytokines  
DNA  
**Growth factors, animal**  
Hormones, animal, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**crosslinked** polysaccharide drug carriers)

IT Drug delivery systems  
(implants; **crosslinked** polysaccharide drug carriers)

IT **9004-54-0D**, Dextran, derivs., **crosslinked**, biological studies **9005-32-7D**, Alginic acid, derivs., **crosslinked** **9005-49-6D**, Heparin, derivs., **crosslinked**, biological studies **9042-14-2D**, Dextran sulfate, derivs., **crosslinked** **9050-30-0D**, Heparan sulfate, derivs., **crosslinked** **9056-36-4D**, Keratan sulfate, derivs., **crosslinked** **24967-94-0D**, Dermatan sulfate, derivs., **crosslinked** **62031-54-3**, Fibroblast growth factor  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**crosslinked** polysaccharide drug carriers)

IT **9004-61-9**, Hyaluronic acid  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of **crosslinked** polysaccharide drug carriers)

IT **9004-61-9DP**, Hyaluronic acid, derivs., **crosslinked** **9007-28-7DP**, Chondroitin sulfate, derivs., **crosslinked** with hyaluronate  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of **crosslinked** polysaccharide drug carriers)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:544101 HCAPLUS

DOCUMENT NUMBER: 125:177462

TITLE: Surface-modified nanoparticles and method of making and using them

INVENTOR(S): Levy, Robert J.; Labhasetwar, Vinod; Song, Cunxian S.

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 170 pp.

CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.                                                                        | KIND | DATE     | APPLICATION NO. | DATE     |
|-----------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 9620698                                                                        | A2   | 19960711 | WO 1996-US476   | 19960104 |
| WO 9620698                                                                        | A3   | 19980122 |                 |          |
| W: AL, AM, AT, AU, CA, CH, CN, CZ, DE, DK, GB, HU, IS, JP, KE, LU, VN, MN, NO, US |      |          |                 |          |
| RW: KE, LS, SD, AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, PT, SE, NL, MR, NE, SN    |      |          |                 |          |
| CA 2207961                                                                        | AA   | 19960711 | CA 1996-2207961 | 19960104 |
| AU 9647556                                                                        | A1   | 19960724 | AU 1996-47556   | 19960104 |
| EP 805678                                                                         | A1   | 19971112 | EP 1996-903476  | 19960104 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE             |      |          |                 |          |
| JP 10511957                                                                       | T2   | 19981117 | JP 1996-521279  | 19960104 |
| PRIORITY APPLN. INFO.:                                                            |      |          |                 |          |
|                                                                                   |      |          | US 1995-369541  | 19950105 |
|                                                                                   |      |          | US 1995-389893  | 19950216 |
|                                                                                   |      |          | WO 1996-US476   | 19960104 |

AB Biodegradable controlled-release nanoparticles as sustained release bioactive agent delivery vehicles include surface modifying agents to target binding of the nanoparticles to tissues or cells of living systems, to enhance nanoparticle sustained release properties, and to protect nanoparticle-incorporated bioactive agents. Unique methods of making small (10 nm to 15 nm, and preferably 20 nm to 35 nm) nanoparticles having a narrow size distribution which can be surface-modified after the nanoparticles are formed is described. Techniques for modifying the surface include a lyophilization technique to produce a phys. adsorbed coating and epoxy-derivatization to functionalize the surface of the nanoparticles to covalently bind mols. of interest. The nanoparticles may also comprise hydroxy-terminated or epoxide-terminated and/or activated multiblock copolymers, having hydrophobic segments which may be polycaprolactone and hydrophilic segments. The nanoparticles are useful for local intravascular administration of smooth muscle inhibitors and antithrombogenic agents as part of interventional cardiac or vascular catheterization such as a balloon angioplasty procedure; direct application to tissues and/or cells for gene therapy, such as the delivery of osteotropic genes or gene segments into bone progenitor cells; or oral administration in an enteric capsule for delivery of protein/peptide based vaccines.

IC A61K009-51

CC 63-6 (Pharmaceuticals)

IT **Animal growth regulators**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (antagonists; surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

IT Alkylating agents, biological

Antibiotics

Anticoagulants and Antithrombotics

Emulsifying agents

Encapsulation

**Freeze drying**

Immunosuppressants

Inflammation inhibitors

Neoplasm inhibitors  
 Sound and Ultrasound  
 Surfactants  
 Thrombolytics  
 Vaccines

(surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

IT **Dental materials and appliances**

(adhesives, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

IT **Animal growth regulators**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**blood platelet-derived growth factors**, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

IT **Animal growth regulators**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**bone morphogenetic proteins**, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

IT **Animal growth regulators**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**transforming growth factors**, surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

IT **62229-50-9, Epidermal growth factor**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(heparin-binding, -like compds.; surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

IT 50-70-4, D-Glucitol, biological studies 57-09-0, Cetyl trimethyl ammonium bromide 57-10-3, Hexadecanoic acid, biological studies 57-88-5, Cholesterol, biological studies 69-65-8, D-Mannitol 102-71-6, Triethanolamine, biological studies 112-02-7, Hexadecyl trimethyl ammonium chloride 151-21-3, Sodium dodecyl sulfate, biological studies 577-11-7, Sodium dioctyl sulfosuccinate 1069-55-2, Isobutyl cyanoacrylate 3282-73-3, Didodecyl dimethyl ammonium bromide 7445-62-7 7727-43-7, Barium sulfate 8007-43-0, Sorbitan sesquioleate 9000-65-1, Tragacanth 9000-69-5, Pectin 9002-89-5, Polyvinyl alcohol 9002-92-0, Polyoxyethylene lauryl ether 9003-39-8, Polyvinyl pyrrolidone 9003-53-6, Polystyrene 9004-32-4 9004-34-6, Cellulose, biological studies 9004-35-7, Cellulose acetate 9004-44-8, Cellulose phthalate 9004-64-2, Hydroxypropyl cellulose 9004-99-3 9005-49-6, Heparin, biological studies **9015-73-0** 9050-04-8, CM-cellulose calcium 9050-31-1, Hydroxypropyl methyl cellulose phthalate 10103-46-5, Calcium phosphate 25322-68-3 106392-12-5, Poloxamer 110617-70-4, Poloxamine 128835-92-7, Lipofectin 180741-27-9

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(surface-modified polymer controlled-release nanoparticles for sustained drug delivery)

IT 50-02-2, Dexamethasone 59-52-9 60-00-4, EDTA, biological studies 60-10-6, Dithizone 77-86-1 77-92-9, biological studies 87-69-4, biological studies 92-84-2D, Phenothiazine, derivs. 102-71-6D, Triethanolamine, fatty acid esters 139-13-9 144-62-7, Ethanedioic acid, biological studies 1306-06-5, Hydroxyapatite 1338-39-2, Span 20 2462-63-7 9000-01-5, Acacia gum 9003-05-8, Polyacrylamide **9004-54-0**, Dextran, biological studies 9005-25-8, Starch,

biological studies 9005-32-7, Alginic acid 9012-76-4, Chitosan  
 10102-43-9D, Nitric oxide, compds. 11128-99-7, Angiotensin II  
 14930-96-2, Cytochalasin B **61912-98-9**, Insulin-like growth  
 factor 81845-44-5, Ciprostone 106096-92-8, Acidic fibroblast growth  
 factor 106096-93-9, Basic fibroblast growth factor 114949-22-3,  
 Activin 122647-31-8, Ibutilide 130736-65-1, U 86983  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (surface-modified polymer controlled-release nanoparticles for  
 sustained drug delivery)

L51 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:358762 HCAPLUS

DOCUMENT NUMBER: 122:170268

TITLE: Biocompatible implants carrying cells using a  
 retroviral expression vector for use in the  
 manufacture and secretion of therapeutic compounds

INVENTOR(S): Moullier, Philippe; Danos, Olivier; Heard,  
 Jean-Michel; Ferry, Nicolas

PATENT ASSIGNEE(S): Institut Pasteur, Fr.

SOURCE: PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                            | KIND | DATE     | APPLICATION NO. | DATE        |
|-----------------------------------------------------------------------|------|----------|-----------------|-------------|
| WO 9424298                                                            | A1   | 19941027 | WO 1994-FR456   | 19940421    |
| W: AU, CA, JP, US                                                     |      |          |                 |             |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE    |      |          |                 |             |
| FR 2704236                                                            | A1   | 19941028 | FR 1993-4700    | 19930421    |
| FR 2704236                                                            | B1   | 19950623 |                 |             |
| FR 2708202                                                            | A1   | 19950203 | FR 1993-9185    | 19930726    |
| FR 2708202                                                            | B1   | 19960329 |                 |             |
| AU 9466812                                                            | A1   | 19941108 | AU 1994-66812   | 19940421    |
| AU 688321                                                             | B2   | 19980312 |                 |             |
| EP 702723                                                             | A1   | 19960327 | EP 1994-914431  | 19940421    |
| EP 702723                                                             | B1   | 20020904 |                 |             |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE |      |          |                 |             |
| JP 08508880                                                           | T2   | 19960924 | JP 1994-522856  | 19940421    |
| EP 1231277                                                            | A2   | 20020814 | EP 2002-3797    | 19940421    |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE |      |          |                 |             |
| AT 223493                                                             | E    | 20020915 | AT 1994-914431  | 19940421    |
| ES 2181717                                                            | T3   | 20030301 | ES 1994-914431  | 19940421    |
| US 5906817                                                            | A    | 19990525 | US 1996-532814  | 19960119    |
| AU 9859675                                                            | A1   | 19980604 | AU 1998-59675   | 19980330    |
| AU 704371                                                             | B2   | 19990422 |                 |             |
| US 6326195                                                            | B1   | 20011204 | US 1999-225509  | 19990106    |
| US 2002098223                                                         | A1   | 20020725 | US 2001-987601  | 20011115    |
| PRIORITY APPLN. INFO.:                                                |      |          | FR 1993-4700    | A 19930421  |
|                                                                       |      |          | FR 1993-9185    | A 19930726  |
|                                                                       |      |          | EP 1994-914431  | A3 19940421 |
|                                                                       |      |          | WO 1994-FR456   | W 19940421  |
|                                                                       |      |          | US 1996-532814  | A3 19960119 |
|                                                                       |      |          | US 1999-225509  | A3 19990106 |

AB Neo-organ implants for use preferably in the peritoneal cavity of the

recipient are described for use in the in situ synthesis and secretion of a therapeutic compd. The implant includes a biocompatible support for anchoring of cells that can secrete a therapeutic compd. embedded in a collagen gel. The cells may naturally synthesize the compd. or they may be transformed with a novel retrovirus expression vector from which the gag, pol, and env genes have been deleted to prevent viral replication. Fibroblasts transformed with a Moloney murine leukemia virus-based expression vector (M48) carrying .beta.-glucuronidase gene under control of the PGK promoter were immobilized on collagen-coated PTFE fibers and incorporated into a collagen gel in the presence of basic fibroblast growth factor. The implant was then introduced into the peritoneal cavity by attachment to the arms of the intestine in contact with the mesentery; the implant did not give rise to an inflammatory response. In animals showing a genetic .beta.-glucuronidase deficiency the implants caused a rapid fall in urinary secretion of intermediates from the catabolism of mucopolysaccharides and a spectacular normalization of the histol. of the liver and spleen.

- IC ICM C12N015-86  
ICS A61K048-00; C12N005-10; A61L027-00; A61K009-14; C12N009-24;  
C12N015-27; C12N009-12; C12N015-12; C12N015-56; C12N015-54
- CC 63-7 (Pharmaceuticals)
- IT **Animal growth regulators**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(angiogenic factors, as angiogenic factor in implants contg. transgenic cells; biocompatible implants carrying cells using a retroviral expression vector for use in the manuf. and secretion of therapeutic compds.)
- IT Collagens, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**crosslinked**, as substrate for immobilization of cells for implants; biocompatible implants carrying cells using a retroviral expression vector for use in the manuf. and secretion of therapeutic compds.)
- IT **Prosthetic materials and Prosthetics**  
(implants, biocompatible implants carrying cells using a retroviral expression vector for use in the manuf. and secretion of therapeutic compds.)
- IT 9002-84-0, PTFE **9004-54-0**, Dextran, biological studies  
9004-61-9, Hyaluronic acid  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(as substrate for immobilization of cells for implants; biocompatible implants carrying cells using a retroviral expression vector for use in the manuf. and secretion of therapeutic compds.)

L51 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1992:91479 HCAPLUS  
DOCUMENT NUMBER: 116:91479  
TITLE: Surgical implant and method incorporating  
chemotherapeutic agents  
INVENTOR(S): Jernberg, Gary R.  
PATENT ASSIGNEE(S): USA  
SOURCE: PCT Int. Appl., 30 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.                                                                                                        | KIND                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | DATE     | APPLICATION NO. | DATE     |
|-------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|----------|
| WO 9117744                                                                                                        | A1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 19911128 | WO 1991-US2784  | 19910423 |
| W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          |                 |          |
| RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          |                 |          |
| CA 2082398                                                                                                        | AA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 19911115 | CA 1991-2082398 | 19910423 |
| AU 9179096                                                                                                        | A1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 19911210 | AU 1991-79096   | 19910423 |
| EP 528971                                                                                                         | A1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 19930303 | EP 1991-910569  | 19910423 |
| EP 528971                                                                                                         | B1                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 19990901 |                 |          |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          |                 |          |
| US 5290271                                                                                                        | A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 19940301 | US 1993-99265   | 19930729 |
| PRIORITY APPLN. INFO.:                                                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          | US 1990-523067  | 19900514 |
|                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          | US 1990-599699  | 19901018 |
|                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          | WO 1991-US2784  | 19910423 |
|                                                                                                                   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          | US 1992-899096  | 19920615 |
| AB                                                                                                                | A surgical implant which provides controlled release and improved cellular uptake of chemotherapeutic agents over a predetd. period of time, is prepd. by incorporating time-release microshapes encapsulating .gtoreq.1 chemotherapeutic agent and carrier agents into a biocompatible implant. The implant can be a vascular graft, heart valve leaflet, artificial skin, etc.                                                                                                                                     |          |                 |          |
| IC                                                                                                                | ICM A61K009-22                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |          |                 |          |
|                                                                                                                   | ICS A61K009-52; A61L027-00                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |          |                 |          |
| CC                                                                                                                | 63-7 (Pharmaceuticals)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |          |                 |          |
| IT                                                                                                                | <b>Animal growth regulators</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |          |                 |          |
|                                                                                                                   | RL: BIOL (Biological study)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |          |                 |          |
|                                                                                                                   | (bone morphogenetic protein, surgical implants contg. microencapsulated)                                                                                                                                                                                                                                                                                                                                                                                                                                             |          |                 |          |
| IT                                                                                                                | Collagens, compounds                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |          |                 |          |
|                                                                                                                   | RL: BIOL (Biological study)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |          |                 |          |
|                                                                                                                   | (crosslinked, prosthetic implant manuf. from, chemotherapeutic agent-encapsulated microspheres incorporation in)                                                                                                                                                                                                                                                                                                                                                                                                     |          |                 |          |
| IT                                                                                                                | <b>Prosthetic materials and Prosthetics</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |          |                 |          |
|                                                                                                                   | (implants, microencapsulated chemotherapeutics in)                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |          |                 |          |
| IT                                                                                                                | <b>Prosthetic materials and Prosthetics</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |          |                 |          |
|                                                                                                                   | (implants, vascular, microencapsulated chemotherapeutics in)                                                                                                                                                                                                                                                                                                                                                                                                                                                         |          |                 |          |
| IT                                                                                                                | 50-02-2, Dexamethasone 50-23-7, Hydrocortisone 50-24-8, Prednisolone 53-06-5, Cortisone 53-86-1, Indomethacin 60-54-8, Tetracycline 114-07-8, Erythromycin 378-44-9, .beta.-Methasone 443-48-1, Metronidazole 644-62-2, Meclofenamic acid 1404-04-2, Neomycin 1404-90-6, Vancomycin 1406-05-9, Penicillin 5104-49-4 8063-07-8, Kanamycin 9004-54-0, Dextran, biological studies 9005-49-6, Heparin, biological studies 11111-12-9, Cephalosporin 15687-27-1, Ibuprofen 22204-53-1, Naproxen 35121-78-9, Prostacyclin |          |                 |          |
|                                                                                                                   | RL: BIOL (Biological study)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |          |                 |          |
|                                                                                                                   | (surgical implants contg. microencapsulated)                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |          |                 |          |

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L7 13610 SEA FILE=HCAPLUS ABB=ON PLU=ON DEXTRAN+NT/CT  
 L11 31790 SEA FILE=HCAPLUS ABB=ON PLU=ON "GROWTH FACTORS, ANIMAL"+OLD/C  
 T  
 L14 24623 SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTHETIC MATERIALS AND  
 PROSTHETICS"+OLD/CT  
 L15 4540 SEA FILE=HCAPLUS ABB=ON PLU=ON BONE FORMATION/CT  
 L16 3800 SEA FILE=HCAPLUS ABB=ON PLU=ON "BONE MORPHOGENETIC PROTEINS"+  
 OLD,NT/CT  
 L17 20049 SEA FILE=HCAPLUS ABB=ON PLU=ON "DENTAL MATERIALS AND  
 APPLIANCES"+OLD/CT  
 L18 117 SEA FILE=HCAPLUS ABB=ON PLU=ON "PROSTHETIC MATERIALS AND  
 PROSTHETICS (L) MAXILLOFACIAL"/CT  
 L24 17023 SEA FILE=HCAPLUS ABB=ON PLU=ON EPIDERMAL GROWTH FACTOR/CT  
 L25 18840 SEA FILE=HCAPLUS ABB=ON PLU=ON "INSULIN-LIKE GROWTH FACTOR"+N  
 T/CT  
 L26 3481 SEA FILE=HCAPLUS ABB=ON PLU=ON "FIBROBLAST GROWTH FACTOR"/CT  
 L27 21413 SEA FILE=HCAPLUS ABB=ON PLU=ON "TRANSFORMING GROWTH FACTORS"+  
 OLD,NT/CT  
 L28 8044 SEA FILE=HCAPLUS ABB=ON PLU=ON "PLATELET-DERIVED GROWTH  
 FACTORS"+OLD,NT/CT  
 L29 3800 SEA FILE=HCAPLUS ABB=ON PLU=ON "BONE MORPHOGENETIC PROTEINS"+  
 OLD,NT/CT  
 L30 51 SEA FILE=HCAPLUS ABB=ON PLU=ON ((L24 OR L25 OR L26 OR L27 OR  
 L28 OR L29) CR L11) AND L7 AND (L14 OR L15 OR L16 OR L17 OR  
 L18)  
 L45 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND CROSSLINK?  
 L47 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND (FREEZEDR? OR FREEZE  
 DR?)  
 L49 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L47 AND HYDROGEL?  
 L51 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L45 OR L47 OR L49  
 L52 18 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 AND (CORAL OR HYDROXYAPATI  
 TE OR TRICALCIC CALCIUM PHOSPHATE OR CALCIUM SULFATE OR  
 CALCIUM CARBONATE)  
 L53 13 SEA FILE=HCAPLUS ABB=ON PLU=ON L52 NOT L51

=&gt; d ibib ab hitind l53 1=13

L53 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2003:300930 HCAPLUS  
 TITLE: Improved bone graft  
 INVENTOR(S): Knaack, David; Traianedes, Kathy; Diegman, Michele;  
 Forsyth, Nanette; Winterbottom, John  
 PATENT ASSIGNEE(S): Osteotech, Inc., USA  
 SOURCE: PCT Int. Appl., 87 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2003030956 | A2   | 20030417 | WO 2002-US32941 | 20021015 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2001-329156P P 20011012

US 2002-392462P P 20020627

AB An improved demineralized bone matrix (DBM) or other matrix compn. is provided that has been mixed with a stabilizing agent that acts as (1) a diffusion barrier, (2) a enzyme inhibitor, (3) a competitive substrate, or (4) a masking moiety. A diffusion barrier acts as a barrier so as to protect the osteoinductive factors found in DBM from being degraded by proteolytic and glycolytic enzymes at the implantation site. Stabilizing agents may be any biodegradable material such as starches, modified starches, cellulose, dextran, polymers, proteins, and collagen. As the stabilizing agents degrades or dissolves in vivo, the osteoinductive factors such as TGF- $\beta$ , BMP, and IGF are activated or exposed, and the activated factors work to recruit cells from the perivascular space to the site of injury and to cause differentiation into bone-forming cells. The invention also provides methods of prepg., testing, and using the inventive improved osteoinductive matrix compns.

ICM A61L027-00

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 9

IT INDEXING IN PROGRESS

IT Alkylating agents, biological

Antibiotics

Antitumor agents

**Bone formation**

Diffusion barrier

Drug delivery systems

Milling (size reduction)

Nutrients

Particle size distribution

Stabilizing agents

Virus

Wound healing promoters

(improved bone graft comprising a demineralized bone matrix)

IT Agglutinins and Lectins

Alkyl iodides

Angiogenic factors

Antibodies

Biopolymers

**Bone morphogenetic proteins**

Fatty acids

Lipids

Phosphatidylcholines

Polyesters

Polyethers

Polymers

Polysaccharides

Proteins



**Transforming growth factors**

RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(improved bone graft comprising a demineralized bone matrix)

**IT Growth factors, animal**

RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(improved bone graft comprising a demineralized bone matrix)

**IT Growth factors, animal**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(improved bone graft comprising a demineralized bone matrix)

**IT Growth factors, animal**

RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(osteogenins; improved bone graft comprising a demineralized bone matrix)

**IT 1306-06-5, Hydroxyapatite 7758-87-4, Tricalcium phosphate**

**7778-18-9, Calcium sulfate 10103-46-5, Calcium phosphate 13767-12-9, Tetracalcium phosphate**

RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ceramics; improved bone graft comprising a demineralized bone matrix)

**IT 50-01-1, Guanidine hydrochloride 64-69-7, Iodoacetic acid 74-88-4, Methyl iodide 3483-12-3, Dithiothreitol 9000-94-6, Antithrombin iii 9002-89-5, Polyvinyl alcohol 9003-16-1, polyfumalic acid 9004-34-6, Cellulose 9004-54-0, Dextran 9005-25-8, starch 26009-03-0, Polyglycolic acid 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 34346-01-5, Lactic acid-glycolic acid copolymer 61912-98-9, Igf 81627-83-0, Mcsf**

RL: DEV (Device component use); TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(improved bone graft comprising a demineralized bone matrix)

L53 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:282718 HCAPLUS

DOCUMENT NUMBER: 138:282352

TITLE: Traversal of nucleic acid molecules through a tissue fluid space and expression in repair cells

INVENTOR(S): Sosnowski, Barbara A.; Pierce, Glenn

PATENT ASSIGNEE(S): Selective Genetics, Inc., USA

SOURCE: PCT Int. Appl., 95 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                         | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2003029429                                                                                                                                                                                                                                                                                                                      | A2   | 20030410 | WO 2002-US31546 | 20021002 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, |      |          |                 |          |

UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,  
 RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2001-327513P P 20011003

- AB Disclosed are methods for use in transferring nucleic acids into cells at a wound site assocd. with a fluid space. These gene transfer protocols are suitable for use in transferring various nucleic acids into cartilage, cardiac muscle, and other tissues, and have many uses including treating diseases such as arthritis and ischemic heart disease, and promoting wound healing. The invention further disclosed pharmaceutical compns. that may be used in the practice of the invention to transfer the nucleic acid of interest. Such compns. include any multi-partitioned biocompatible matrix in combination with multiple nucleic acids of interest. Thus, collagen collagen-immobilized fibroblast growth factor (FGF) genes induce angiogenesis in vitro, and FGF gene delivery to skeletal muscle wounds induces both angiogenesis and arteriogenesis and well as induces myocyte regeneration.
- IC ICM C12N
- CC 3-2 (Biochemical Genetics)  
 Section cross-reference(s): 1
- IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (10, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (2, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (3, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (4, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (5, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (6, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (7, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (8, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (9, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Prosthetic materials and Prosthetics**  
(bioactive glass, biocompatible; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Growth factors, animal**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(chondromodulins, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT Angiogenesis  
**Bone formation**  
Regeneration, animal  
Wound healing  
(gene therapy for stimulation of; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gene therapy with nucleic acids encoding BMP-12; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Bone morphogenetic proteins**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gene therapy with nucleic acids encoding BMP-13; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT Antibodies  
**Bone morphogenetic proteins**  
Growth factor receptors  
**Growth factors, animal**  
Hepatocyte growth factor  
Hormones, animal, biological studies  
Insulin-like growth factor receptors  
Interleukin 1  
Interleukin 6  
Interleukin 8  
Interleukins  
Leukemia inhibitory factor  
**Platelet-derived growth factors**  
Transcription factors  
**Transforming growth factors**  
Tumor necrosis factors  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Growth factors, animal**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(skeletal growth factors, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Transforming growth factors**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.alpha.-, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)
- IT **Transforming growth factors**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.1-, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in

repair cells)

IT **Transforming growth factors**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(.beta.2-, gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT 1306-06-5, **Hydroxyapatite** 9002-84-0, Polytetrafluoroethylene 9002-88-4, Polyethylene 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-20-7, Polyvinylacetate 9004-34-6, Cellulose, biological studies **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronan 9004-67-5, Methyl cellulose 9005-32-7, Alginate acid 9012-76-4, Chitosan 9016-00-6, Poly(dimethylsiloxane) 11098-82-1, Aluminate 24937-78-8, Poly(ethylene-vinyl acetate) 25322-68-3, Polyethylene glycol 25852-47-5, Hydrogel 26100-51-6, Lactic acid polymer 26124-68-5, Glycolic acid polymer 31900-57-9, Poly(dimethylsiloxane) 34346-01-5, Lactic acid-Glycolic acid copolymer 124586-38-5, Hydrogel

RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(biocompatible; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

IT 9001-27-8, Blood-coagulation factor VIII 9001-28-9, Blood-coagulation factor IX 9002-64-6, Parathyroid hormone 9002-72-6, Growth hormone 11096-26-7, Erythropoietin 57285-09-3, Inhibin **61912-98-9**, Insulin-like growth factor **62031-54-3**, Fibroblast growth factor **62229-50-9**, Epidermal growth factor **67763-96-6**, Insulin-like growth factor I **67763-97-7**, Insulin-like growth factor II 81627-83-0, Macrophage-colony stimulating factor 83869-56-1, Granulocyte-macrophage-colony stimulating factor 103370-86-1, Parathyroid hormone-related peptide 106096-93-9, Basic fibroblast growth factor 114949-22-3, Activin 127464-60-2, Vascular endothelial growth factor 139639-23-9, Tissue plasminogen activator 189460-40-0, Connective tissue-growth factor 252959-51-6, Growth differentiation factor 11

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(gene therapy with nucleic acids encoding; traversal of nucleic acid mols. through a tissue fluid space and expression in repair cells)

L53 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:906235 HCAPLUS

DOCUMENT NUMBER: 136:25166

TITLE: Method for composite cell-based implants using mineral or polymeric microcarriers

INVENTOR(S): Frondoza, Carmelita G.; Hungerford, David S.; Shikani, Alan H.; Domb, Abraham J.; Fink, David J.; Bloom, Leonard

PATENT ASSIGNEE(S): Chondros, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U. S. Ser. No. 825,632.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE  | APPLICATION NO. | DATE  |
|------------|------|-------|-----------------|-------|
| -----      | ---- | ----- | -----           | ----- |

|               |    |          |                |          |
|---------------|----|----------|----------------|----------|
| US 2001051834 | A1 | 20011213 | US 2001-922909 | 20010806 |
| US 2001014475 | A1 | 20010816 | US 2001-825632 | 20010404 |
| US 2002012705 | A1 | 20020131 | US 2001-929697 | 20010814 |
| US 6514522    | B2 | 20030204 |                |          |
| US 2002123142 | A1 | 20020905 | US 2002-39718  | 20020103 |

PRIORITY APPLN. INFO.:

|                 |    |          |
|-----------------|----|----------|
| US 1998-81016P  | P  | 19980408 |
| US 1998-104842P | P  | 19981020 |
| US 1999-275319  | A2 | 19990324 |
| US 2000-712662  | A2 | 20001114 |
| US 2001-825632  | A2 | 20010404 |
| US 1999-165608P | P  | 19991115 |
| US 2000-228855P | P  | 20000829 |

AB This invention is a method for the implantation of a combination of cells or cell-microcarrier aggregates wherein one component comprises a solid implantable construct and a second component comprises an injectable formulation. For example, in one embodiment, the solid implant may be first implanted to fill the majority of the cavity receiving the implant, and then cells or cell-microcarrier aggregates in an injectable format, with or without the addn. of gelling materials to promote rapid gelling in situ, may be injected into spaces surrounding the solid implant in order to secure the solid implant in the site and/or to promote rapid adherence and/or integration of the solid implant to surrounding tissues. Also contemplated in this embodiment is that the cellular compn. of the injectable component may differ from that of the solid component. For example, the solid implant may result from the culturing of chondrocytes on microcarriers or scaffolds, e.g., **calcium carbonate**, calcium phosphate or **calcium sulfate**, biopolymers, or synthetic polymers such as polylactic acid, polyglycolic or their copolymers, thereby resulting in an implant having cartilage-like properties, whereas the injectable cells or aggregates may result from the culturing of stem cells, resulting thereby in cells capable of producing cells of a chondrogenic, fibroblastic, myoblastic or osteoblastic phenotype. In this example, cells in the injectable aggregates may promote the fixation to or rapid integration of the solid cartilage implant into surrounding cartilage, connective tissue, muscle or bone, resp. A method of treating a skin lesion or nose or ear defects comprises filling the lesion or defect with a solid cell-contg. implant along with an injectable cell-contg. formulation.

IC ICM A61F002-02

ICS A61F002-28

NCL 623023720

CC 63-7 (Pharmaceuticals)

IT Antibodies

**Bone morphogenetic proteins**

Cytokines

**Growth factors, animal**

Integrins

Interleukins

Lymphotoxin

**Platelet-derived growth factors**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(fluid medium for injection contg.; composite of solid implant and injectable formulation of cells or cell-microcarrier aggregates for tissue repair)

IT **Prosthetic materials and Prosthetics**

(implants; composite of solid implant and injectable formulation of cells or cell-microcarrier aggregates for tissue repair)

IT **62031-54-3**, Fibroblast growth factor  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (fluid medium for injection contg.; composite of solid implant and  
 injectable formulation of cells or cell-microcarrier aggregates for  
 tissue repair)

IT 471-34-1, **Calcium carbonate**, biological studies  
 1398-61-4, Chitin 7778-18-9, **Calcium sulfate**  
 9002-89-5, Polyvinyl alcohol 9002-98-6 9003-01-4, Poly(acrylic acid)  
**9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic  
 acid 9005-35-0, Calcium alginate 9012-36-6, Agarose 9012-76-4,  
 Chitosan 10103-46-5, Calcium phosphate 24980-41-4, Polycaprolactone  
 25248-42-4, Polycaprolactone 25322-68-3, Polyethylene glycol  
 26009-03-0, Polyglycolic acid 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-  
 ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid  
 34346-01-5, Glycolic acid-lactic acid copolymer  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (microcarriers or scaffolds; composite of solid implant and injectable  
 formulation of cells or cell-microcarrier aggregates for tissue repair)

L53 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:618469 HCAPLUS

DOCUMENT NUMBER: 135:170821

TITLE: Osteogenic devices and methods of use thereof for  
 repair of endochondral bone and osteochondral and  
 chondral defects

INVENTOR(S): Rueger, David C.; Tucker, Marjorie A.; Chang, An-Cheng

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 59 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
| US 2001016646          | A1   | 20010823 | US 1998-45331   | 19980320 |
| PRIORITY APPLN. INFO.: |      |          | US 1998-45331   | 19980320 |

AB Disclosed herein are improved osteogenic devices and methods of use  
 thereof for repair of bone and cartilage defects. The devices and methods  
 promote accelerated formation of repair tissue with enhanced stability  
 using less osteogenic protein than devices in the art. Defects  
 susceptible to repair with the instant invention include, but are not  
 limited to: crit. size defects, non-crit. size defects, non-union  
 fractures, fractures, osteochondral defects, subchondral defects, and  
 defects resulting from degenerative diseases such as osteochondritis  
 dissecans.

IC ICM C07K001-00

ICS C07K014-00; C07K017-00; A01N025-34; G01N033-53

NCL 530840000

CC 63-7 (Pharmaceuticals)

IT **Bone morphogenetic proteins**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); PEP (Physical, engineering or chemical process); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(10; osteogenic devices for repair of endochondral bone and  
 osteochondral and chondral defects)

- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(11; osteogenic devices for repair of endochondral bone and osteochondral and chondral defects)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(12; osteogenic devices for repair of endochondral bone and osteochondral and chondral defects)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(15; osteogenic devices for repair of endochondral bone and osteochondral and chondral defects)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(16; osteogenic devices for repair of endochondral bone and osteochondral and chondral defects)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(3; osteogenic devices for repair of endochondral bone and osteochondral and chondral defects)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(4; osteogenic devices for repair of endochondral bone and osteochondral and chondral defects)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(5; osteogenic devices for repair of endochondral bone and osteochondral and chondral defects)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(6; osteogenic devices for repair of endochondral bone and osteochondral and chondral defects)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(7; osteogenic devices for repair of endochondral bone and osteochondral and chondral defects)
- IT **Bone morphogenetic proteins**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(7; osteogenic devices for repair of endochondral bone and osteochondral and chondral defects)

(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(9; osteogenic devices for repair of endochondral bone and  
osteochondral and chondral defects)

## IT Binders

**Bone formation**

Protein sequences

Wetting agents

cDNA sequences

(osteogenic devices for repair of endochondral bone and osteochondral  
and chondral defects)

IT **Growth factors, animal**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); PEP (Physical, engineering or chemical process); THU  
(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(osteogenic protein 2; osteogenic devices for repair of endochondral  
bone and osteochondral and chondral defects)

IT **Growth factors, animal**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); PEP (Physical, engineering or chemical process); THU  
(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(osteogenic protein 3; osteogenic devices for repair of endochondral  
bone and osteochondral and chondral defects)

IT 69-65-8, mannitol 9004-32-4, carboxymethylcellulose 9004-34-6D,  
cellulose, alkyl derivs., biological studies **9004-54-0**, dextran,  
biological studies 9004-62-0, Hydroxyethylcellulose 9004-65-3,  
hydroxypropylmethylcellulose 9004-67-5, methylcellulose 9032-42-2,  
methylhydroxyethylcellulose  
RL: DEV (Device component use); MOA (Modifier or additive use); PEP  
(Physical, engineering or chemical process); THU (Therapeutic use); BIOL  
(Biological study); PROC (Process); USES (Uses)  
(osteogenic devices for repair of endochondral bone and osteochondral  
and chondral defects)

IT 1306-06-5, **hydroxyapatite** 7758-87-4, tricalcium phosphate  
RL: DEV (Device component use); PEP (Physical, engineering or chemical  
process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);  
USES (Uses)  
(osteogenic devices for repair of endochondral bone and osteochondral  
and chondral defects)

L53 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:581931 HCAPLUS

DOCUMENT NUMBER: 135:157661

TITLE: Extraction of growth factors from tissue

INVENTOR(S): Donda, Russell S.; Wironen, John F.; Seid, Christopher

PATENT ASSIGNEE(S): Regeneration Technologies, Inc., USA

SOURCE: PCT Int. Appl., 12 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2001057082 | A2   | 20010809 | WO 2001-US3474  | 20010202 |
| WO 2001057082 | A3   | 20020221 |                 |          |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,



CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,  
 IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,  
 MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,  
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,  
 BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001041792 A1 20011115 US 2001-776619 20010202

PRIORITY APPLN. INFO.:

US 2000-180067P P 20000203

US 2000-200842P P 20000501

US 2000-215912P P 20000703

AB Disclosed are novel methods of obtaining osteogenic and other growth factor compns. from alternative nonbone sources such as tissue or bone marrow, and methods of using the same. Also disclosed are implants infused with growth factors obtained from the methods. An example is given of extn. of growth factors from platelets.

IC ICM C07K014-475

CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 2

IT **Prosthetic materials and Prosthetics**

(bioactive glass; extn. of growth factors from tissue)

IT **Prosthetic materials and Prosthetics**

(ceramics; extn. of growth factors from tissue)

IT **Platelet-derived growth factors**

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); USES (Uses)  
 (extn. of growth factors from tissue)

IT **Growth factors, animal**

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)  
 (extn. of growth factors from tissue)

IT **Prosthetic materials and Prosthetics**

(implants; extn. of growth factors from tissue)

IT Angiogenic factors

**Bone morphogenetic proteins**

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); USES (Uses)  
 (platelet-derived; extn. of growth factors from tissue)

IT 50-01-1, Guanidine hydrochloride 56-81-5, Glycerol, processes 57-13-6, Urea, processes 151-21-3, Sodium dodecyl sulfate, processes 9002-93-1, Triton x100 9004-34-6, Cellulose, processes **9004-54-0**, Dextran, processes 9004-61-9, Hyaluronic acid 9005-80-5, Inulin 9012-36-6, Agarose 9037-22-3, Amylopectin 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 26009-03-0, Polyglycolic acid 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 106392-12-5, pluronic F127

RL: PEP (Physical, engineering or chemical process); PROC (Process)  
 (extn. of growth factors from tissue)

IT 1306-06-5, **Hydroxyapatite** 7758-87-4, Tricalcium phosphate  
 7778-18-9, **Calcium sulfate** 10103-46-5, Calcium phosphate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(extn. of growth factors from tissue)

IT **62229-50-9P**, egf

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process); USES (Uses)  
(platelet-derived; extn. of growth factors from tissue)

L53 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:489907 HCAPLUS

DOCUMENT NUMBER: 135:81959

TITLE: Gene transfer to intervertebral disc cells, and use in the treatment of degenerative disk disorders, and animal model for degenerative disk disease

INVENTOR(S): Kang, James D.; Evans, Christopher H.; Nishida, Kotaro; Robbins, Paul D.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 16 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.             | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------|------|----------|-----------------|----------|
| US 2001006948          | A1   | 20010705 | US 1998-199978  | 19981125 |
| PRIORITY APPLN. INFO.: |      |          | US 1998-199978  | 19981125 |

AB Methods for transferring a gene to an intervertebral disk are disclosed. The methods find application in the treatment of patients for degenerative disk disorders, by use of a gene encoding a product that imparts a therapeutic and/or prophylactic benefit. The methods also find application in the establishment of an animal model for the study of degenerative disk disease. A genetically modified intervertebral disk cell is also disclosed.

IC ICM A61K048-00

NCL 514044000

CC 63-5 (Pharmaceuticals)

Section cross-reference(s): 14

IT **Bone morphogenetic proteins**

**Growth factors, animal**

Interleukin 1 receptor antagonist

**Transforming growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(gene transfer to intervertebral disk cells, and use in treatment of degenerative disk disorders, and animal model for degenerative disk disease)

IT **Transforming growth factors**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(.beta.1-; gene transfer to intervertebral disk cells, and use in treatment of degenerative disk disorders, and animal model for degenerative disk disease)

- IT **61912-98-9**, Insulin-like growth factor **62031-54-3**,  
 Fibroblast growth factor 86102-31-0, Tissue inhibitor of  
 metalloproteinase 96282-35-8 105844-41-5, Plasminogen activator  
 inhibitor  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)  
 (gene transfer to intervertebral disk cells, and use in treatment of  
 degenerative disk disorders, and animal model for degenerative disk  
 disease)
- IT 1306-06-5, **Hydroxyapatite** 7758-87-4, Tricalcium phosphate  
 7778-18-9, **Calcium sulfate** 9012-76-4, Chitosan  
 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6,  
 Polylactic acid  
 RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological  
 study); USES (Uses)  
 (gene transfer to intervertebral disk cells, and use in treatment of  
 degenerative disk disorders, and animal model for degenerative disk  
 disease)
- IT **9015-73-0** 10103-46-5, Calcium phosphate  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (gene transfer to intervertebral disk cells, and use in treatment of  
 degenerative disk disorders, and animal model for degenerative disk  
 disease)

L53 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:472523 HCAPLUS  
 DOCUMENT NUMBER: 135:66255  
 TITLE: Liquid composition of a biodegradable block copolymer  
 for drug delivery system  
 INVENTOR(S): Seo, Min-hyo; Choi, In-ja  
 PATENT ASSIGNEE(S): Samyang Corp., S. Korea  
 SOURCE: PCT Int. Appl., 37 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.             | KIND                                                                                                                                                                                                                                                                                                                                                                       | DATE     | APPLICATION NO. | DATE       |
|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------|------------|
| WO 2001045742          | A1                                                                                                                                                                                                                                                                                                                                                                         | 20010628 | WO 2000-KR1508  | 20001221   |
| W:                     | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |          |                 |            |
| RW:                    | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG                                                                                                                                                                                     |          |                 |            |
| EP 1244471             | A1                                                                                                                                                                                                                                                                                                                                                                         | 20021002 | EP 2000-989005  | 20001221   |
| R:                     | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR                                                                                                                                                                                                                                                                     |          |                 |            |
| US 2003082234          | A1                                                                                                                                                                                                                                                                                                                                                                         | 20030501 | US 2002-169012  | 20020622   |
| PRIORITY APPLN. INFO.: |                                                                                                                                                                                                                                                                                                                                                                            |          | KR 1999-60349   | A 19991222 |
|                        |                                                                                                                                                                                                                                                                                                                                                                            |          | WO 2000-KR1508  | W 20001221 |

- AB The present invention relates to a liq. polymeric compn. capable of forming a physiol. active substance-contg. implant when it is injected into a living body and a method of prepn. The compn. comprises a water-sol. biocompatible liq. polyethylene glycol deriv., a biodegradable block copolymer which is insol. in water but sol. in the water-sol. biocompatible liq. polyethylene glycol deriv. and a physiol. active substance. Thus, a triblock copolymer was prepd. from lactide-1,4-dioxanone and PEG. Piroxicam 150, the above biodegradable block copolymer 400, diacetyl polyethylene glycol 420, and gelatin 30 mg were dissolved in a 50% aq. HOAc soln. and the drug-contg. liq. polymeric compn. was filtered and the org. solvent was removed.
- IC ICM A61K047-30
- CC 63-6 (Pharmaceuticals)
- Section cross-reference(s): 37
- IT **Bone morphogenetic proteins**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (liq. compn. of biodegradable block copolymer for drug delivery system)
- IT **Platelet-derived growth factors**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (liq. compn. of biodegradable block copolymer for drug delivery system)
- IT 50-70-4, Sorbitol, biological studies 50-76-0, Actinomycin-D 50-78-2, Aspirin 50-99-7, Glucose, biological studies 51-21-8, 5-Fluorouracil 53-86-1, Indomethacin 57-48-7, Fructose, biological studies 57-50-1, Sucrose, biological studies 59-01-8, Kanamycin 59-05-2, Methotrexate 59-23-4, Galactose, biological studies 60-54-8, Tetracycline 63-42-3, Lactose 69-53-4, Ampicillin 69-65-8, Mannitol 87-79-6, Sorbose 87-99-0, Xylitol 99-20-7, Trehalose 103-90-2, Acetaminophen 114-07-8, Erythromycin 151-21-3, Sodium dodecylsulfate, biological studies 471-34-1, **Calcium carbonate**, biological studies 557-34-6, Zinc acetate 564-25-0, Doxycycline 1066-17-7, colistin 1309-42-8, Magnesium hydroxide 1314-13-2, Zinc oxide, biological studies 1403-66-3, Gentamycin 1404-00-8, Mitomycin 1404-04-2, Neomycin 1404-90-6, Vancomycin 1405-87-4, bacitracin 1406-05-9, Penicillin 1407-47-2, angiotensin 3486-35-9, Zinc carbonate 5104-49-4, Flurbiprofen 6990-06-3, Fusidic acid 7446-70-0, Aluminum chloride, biological studies 7542-37-2, Paromomycin 7646-85-7, Zinc chloride, biological studies 7647-14-5, Sodium chloride, biological studies 7786-30-3, Magnesium chloride, biological studies 9001-63-2, Lysozyme 9002-72-6, Somatotropin 9003-39-8, Polyvinylpyrrolidone 9004-10-8, insulin, biological studies 9004-32-4, Sodium carboxymethyl cellulose **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic acid 9007-12-9, calcitonin 9007-92-5, glucagon, biological studies 9012-76-4, Chitosan 9034-39-3, growth hormone releasing factor 9034-40-6, LHRH 9061-61-4, nerve growth factor 10043-52-4, Calcium chloride, biological studies 10118-90-8, Minocycline 11056-06-7, Bleomycin 11096-26-7, erythropoietin 11111-12-9, Cephalosporin 12619-70-4, Cyclodextrin 13614-98-7, Minocycline hydrochloride 15307-79-6, Diclofenac sodium 15307-86-5, Diclofenac 15663-27-1, Cisplatin 15687-27-1, Ibuprofen 16039-53-5, Zinc lactate 20830-81-3, Daunorubicin 21645-51-2, Aluminum hydroxide, biological studies 22071-15-4, Ketoprofen 22204-53-1, Naproxen 23155-02-4, Phosphomycin 23214-92-8, Doxorubicin 24305-27-9, thyrotropin releasing hormone 25316-40-9, Adriamycin 25322-68-3D, alkyl ethers 25496-72-4, Glyceryl monooleate 29679-58-1, Fenoprofen 31566-31-1, Glyceryl monostearate 32986-56-4, Tobramycin 33069-62-4, Paclitaxel 34493-98-6, Dibekacin 36322-90-4, Piroxicam 37517-28-5, Amikacin 40828-46-4, Suprofen 41575-94-4, Carboplatin 51110-01-1, somatostatin 52093-21-7,

Micronomicin 53994-73-3, Cephaclor 58957-92-9, Idarubicin  
 59804-37-4, Tenoxicam 59995-64-1, Thienamycin 60118-07-2, endorphin  
**62229-50-9**, EGF 63527-52-6 64221-86-9, Imipenem 68767-14-6,  
 Loxoprofen 74011-58-8, Enoxacin 81627-83-0, M-CSF 82419-36-1,  
 Ofloxacin 85721-33-1, Ciprofloxacin 86090-08-6, angiostatin  
 100986-85-4, Levofloxacin 106392-12-5, Poloxamer 114977-28-5, Taxotere  
 126467-48-9, porcine growth hormone 143011-72-7, GCSF 187888-07-9,  
 endostatin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(liq. compn. of biodegradable block copolymer for drug delivery system)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:416980 HCAPLUS

DOCUMENT NUMBER: 135:15095

TITLE: In situ bioreactors expressing systematically  
 available bioactive agents and methods of use thereof  
 in therapy

INVENTOR(S): Pierce, Glenn; Chandler, Lois Ann

PATENT ASSIGNEE(S): Selective Genetics, Inc., USA

SOURCE: PCT Int. Appl., 69 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|---------------|------|----------|-----------------|----------|
| WO 2001040272 | A2   | 20010607 | WO 2000-US32754 | 20001130 |
| WO 2001040272 | A3   | 20020117 |                 |          |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001044413 A1 20011122 US 2000-729644 20001130

PRIORITY APPLN. INFO.: US 1999-168470P P 19991201

AB The present invention relates to a method of in vivo, sustained gene  
 therapy wherein one or more in situ bioreactors (or neo-organoids) express  
 systematically available bioactive agents. One method involves implanting  
 or placing into a tissue site a biocompatible substance capable of  
 cellular ingrowth (e.g., device, matrix, semi-permeable membrane with a  
 matrix or liq. interior, etc.). and systemic delivery of a bioactive  
 factor. Also provided are compns., devices, and kits comprising the same.  
 In various embodiments the biocompatible substance comprises a matrix and  
 at least one nucleic acid mol. encoding a bioactive agent. In other  
 embodiments bioreactors are provided wherein a first gene that encodes a  
 growth factor is present and a second gene encoding a bioactive agent is  
 present during manuf. or provided to the bioreactor following manuf. or  
 implantation.

IC ICM C07K014-00

- CC 3-2 (Biochemical Genetics)  
Section cross-reference(s): 9, 63
- IT **Platelet-derived growth factors**  
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL  
(Biological study); PREP (Preparation); USES (Uses)  
(PDGF-B, as cell growth stimulating agent; in situ bioreactors  
expressing systematically available bioactive agents and methods of use  
thereof in therapy)
- IT Angiogenic factors  
Antisense oligonucleotides  
**Bone morphogenetic proteins**  
Cell adhesion molecules  
Chemotactic factors  
Cytokines  
Hepatocyte growth factor  
Macrophage migration inhibitory factor  
Ribozymes  
**Transforming growth factors**  
p53 (protein)  
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL  
(Biological study); PREP (Preparation); USES (Uses)  
(as cell growth stimulating agent; in situ bioreactors expressing  
systematically available bioactive agents and methods of use thereof in  
therapy)
- IT **Prosthetic materials and Prosthetics**  
(bioactive glass, as biocompatible substance; in situ bioreactors  
expressing systematically available bioactive agents and methods of use  
thereof in therapy)
- IT **Prosthetic materials and Prosthetics**  
(ceramics, alumina, Bioceram, as biocompatible substance; in situ  
bioreactors expressing systematically available bioactive agents and  
methods of use thereof in therapy)
- IT **Transforming growth factors**  
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL  
(Biological study); PREP (Preparation); USES (Uses)  
(.beta.1-, as cell growth stimulating agent; in situ bioreactors  
expressing systematically available bioactive agents and methods of use  
thereof in therapy)
- IT **Transforming growth factors**  
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL  
(Biological study); PREP (Preparation); USES (Uses)  
(.beta.2-, as cell growth stimulating agent; in situ bioreactors  
expressing systematically available bioactive agents and methods of use  
thereof in therapy)
- IT **Transforming growth factors**  
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL  
(Biological study); PREP (Preparation); USES (Uses)  
(.beta.3-, as cell growth stimulating agent; in situ bioreactors  
expressing systematically available bioactive agents and methods of use  
thereof in therapy)
- IT 9004-34-6, Cellulose, biological studies **9004-54-0**, Dextran,  
biological studies 9004-61-9, Hyaluronic acid 9012-76-4, chitosan  
RL: BUU (Biological use, unclassified); DEV (Device component use); BIOL  
(Biological study); USES (Uses)  
(as biocompatible substance (biol. matrix); in situ bioreactors  
expressing systematically available bioactive agents and methods of use  
thereof in therapy)

IT 1306-06-5, **hydroxyapatite** 9005-32-7, Alginic acid  
 11098-82-1, aluminate 24937-78-8, polyethylene vinyl acetate  
 RL: BUU (Biological use, unclassified); DEV (Device component use); BIOL  
 (Biological study); USES (Uses)  
 (as biocompatible substance; in situ bioreactors expressing  
 systematically available bioactive agents and methods of use thereof in  
 therapy)

IT 61912-98-9P, IGF 62031-54-3P, FGF 62229-50-9P,  
 EGF 62683-29-8P, Colony-stimulating factor 127464-60-2P, Vascular  
 endothelial growth factor 250740-90-0P, Angiopoietin  
 RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL  
 (Biological study); PREP (Preparation); USES (Uses)  
 (as cell growth stimulating agent; in situ bioreactors expressing  
 systematically available bioactive agents and methods of use thereof in  
 therapy)

L53 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:493334 HCAPLUS  
 DOCUMENT NUMBER: 133:125276  
 TITLE: Sustained delivery of polyionic bioactive agents  
 INVENTOR(S): Levy, Robert J.  
 PATENT ASSIGNEE(S): The Children's Hospital of Philadelphia, USA  
 SOURCE: PCT Int. Appl., 74 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | KIND | DATE     | APPLICATION NO. | DATE     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2000041647                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | A1   | 20000720 | WO 2000-US1317  | 20000119 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,<br>CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,<br>IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,<br>MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,<br>SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,<br>AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,<br>DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,<br>CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG |      |          |                 |          |
| US 6395029                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | B1   | 20020528 | US 1999-234011  | 19990119 |

PRIORITY APPLN. INFO.: US 1999-234011 A 19990119

AB The invention relates to compns. and methods for delivering a polyionic bioactive compn. such as a nucleic acid to a tissue of an animal. The compns. of the invention include compns. which comprise a matrix comprising the polyionic bioactive agent and wherein at least most of the polyionic bioactive agent at the exterior portion of the matrix is present in a condensed form. The invention also includes methods of making such compns., including particles, devices, bulk materials, and other objects which comprise, consist of, or are coated with such compns. Methods of delivering a polyionic bioactive agent to an animal tissue are also described. The invention further includes a method of storing a nucleic acid.

IC ICM A61F002-02  
 ICS A61F002-06; A61F013-00; A61K009-14; A61K009-16; A61K009-127;  
 A61K047-00; A61K047-48

CC 63-5 (Pharmaceuticals)

IT Drug delivery systems

**Prosthetic materials and Prosthetics**  
(implants; sustained delivery of nucleic acids and other polyionic bioactive agents)

IT Antisense oligonucleotides

**Bone morphogenetic proteins**

Cocoa butter

DNA

Ethylene-propylene rubber

Fluoropolymers, biological studies

Neoprene rubber, biological studies

Nitrile rubber, biological studies

**Platelet-derived growth factors**

Polyamides, biological studies

Polyanhydrides

Polycarbonates, biological studies

Polyesters, biological studies

Polyimides, biological studies

Polyoxyalkylenes, biological studies

Polysulfones, biological studies

Polyurethanes, biological studies

RNA

Rayon, biological studies

Ribozymes

Silicone rubber, biological studies

Stem cell factor

Waxes

cDNA

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(sustained delivery of nucleic acids and other polyionic bioactive agents)

IT **Transforming growth factors**

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(.beta.-; sustained delivery of nucleic acids and other polyionic bioactive agents)

IT 97-90-5, Ethylene glycol dimethacrylate 1306-06-5,  
**Hydroxyapatite** 6606-65-1 7440-06-4, Platinum, biological studies 7440-32-6, Titanium, biological studies 7758-87-4, Tricalcium phosphate 9002-06-6, Thymidine kinase 9002-64-6, Pth 9002-72-6, Growth hormone 9002-84-0, Polytetrafluoroethylene 9002-86-2, Polyvinyl chloride 9002-88-4, Polyethylene 9003-01-4, Polyacrylic acid 9003-05-8, Polyacrylamide 9003-07-0, Polypropylene 9003-17-2, Polybutadiene 9003-18-3, Acrylonitrile butadiene copolymer 9003-20-7, Polyvinylacetate 9003-27-4, Polyisobutylene 9003-31-0, Polyisoprene 9003-39-8, Polyvinylpyrrolidone 9003-42-3, Polyethylmethacrylate 9003-53-6, Polystyrene 9003-56-9, Acrylonitrile butadiene styrene copolymer 9004-35-7, Cellulose acetate 9004-53-9, Dextrin **9004-54-0**, Dextran, biological studies 9005-32-7, Alginic acid 9011-14-7, Polymethylmethacrylate 9012-36-6, Agarose 9016-80-2, Polymethylpentene 9017-21-4, Polymethylstyrene 9046-31-5, Polystyrene carboxylic acid 10586-17-1, Isopropyl cyanoacrylate 12597-68-1, Stainless steel, biological studies 15802-18-3D, Cyanoacrylic acid, polyalkyl derivs. 21982-30-9, Hydroxymethyl methacrylate 24937-78-8, Ethylene vinyl acetate copolymer 24980-41-4, Polycaprolactone



24981-14-4, Polyvinyl fluoride 25068-26-2, Polymethylpentene  
 25087-26-7, Polymethacrylic acid 25102-52-7, Butadiene-isoprene  
 copolymer 25248-42-4, Polycaprolactone 26009-03-0, Polyglycolic acid  
 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6,  
 Polylactic acid 26124-68-5, Polyglycolic acid 50851-57-5, Polystyrene  
 sulfonic acid 61128-18-5, Caprolactone-glycolic acid copolymer  
**61912-98-9**, Insulin-like growth factor **62031-54-3**, Fgf  
 80137-67-3, Caprolactone-lactic acid copolymer 139639-23-9, Tissue  
 plasminogen activator  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic  
 use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (sustained delivery of nucleic acids and other polyionic bioactive  
 agents)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:249066 HCAPLUS

DOCUMENT NUMBER: 130:287100

TITLE: Hydraulic surgical cements comprising calcium  
 phosphate

INVENTOR(S): Lemaitre, Jaques; Bohner, Marc; Van Landuyt, Pascale

PATENT ASSIGNEE(S): H. C. Robert Mathys Stiftung, Switz.; Stratec Medical  
 A.-G.

SOURCE: PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                    | KIND | DATE     | APPLICATION NO. | DATE     |
|-------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 9917710                                                                    | A1   | 19990415 | WO 1998-EP6330  | 19981006 |
| W: CA, JP, US                                                                 |      |          |                 |          |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,<br>PT, SE |      |          |                 |          |
| CA 2306562                                                                    | AA   | 19990415 | CA 1998-2306562 | 19981006 |
| EP 1023032                                                                    | A1   | 20000802 | EP 1998-954344  | 19981006 |
| EP 1023032                                                                    | B1   | 20020102 |                 |          |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE, MC, PT, IE, FI         |      |          |                 |          |
| JP 2001518359                                                                 | T2   | 20011016 | JP 2000-514603  | 19981006 |
| AT 211379                                                                     | E    | 20020115 | AT 1998-954344  | 19981006 |
| ES 2170533                                                                    | T3   | 20020801 | ES 1998-954344  | 19981006 |
| US 6425949                                                                    | B1   | 20020730 | US 2000-529054  | 20000707 |

PRIORITY APPLN. INFO.: WO 1997-EP5495 A 19971007

WO 1998-EP6330 W 19981006

AB The cement for surgical purposes comprises three components. The first  
 component comprises .beta.-Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub> (.beta.-TCP) particles; and  
 Ca(H<sub>2</sub>PO<sub>4</sub>)<sub>2</sub> (MCPA) or Ca(H<sub>2</sub>PO<sub>4</sub>)<sub>2</sub>.cntdot.H<sub>2</sub>O (MCPM) particles or phosphoric  
 acid. The second component comprises water. The third component  
 comprises particles having an av. diam. which is larger than the av. diam.  
 of the .beta.-TCP particles of the first component. Upon mixing of the  
 three components a hardened mass comprising brushite CaHPO<sub>4</sub>.cntdot.2H<sub>2</sub>O  
 (DCPD) is formed. The .beta.-TCP particles have a sp. surface area of  
 less than 10,000 m<sup>2</sup>/g and a Ca/P at. ratio different from 1.50. The  
 component constitutes 1-99 % of the hardened mass. The cements according

to the invention may be used in dental and maxillofacial surgery (alveolar ridge reconstruction, dental socket filling), for orthopedic applications (bone fracture repair, bone augmentation) and for local drug delivery (antibiotics, anti-inflammatory and anti-cancer drugs).

IC ICM A61K006-033

ICS A61L025-00; A61L027-00

CC 63-7 (Pharmaceuticals)

IT **Growth factors, animal**

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(bone-derived, for drug delivery; hydraulic surgical cements comprising calcium phosphate and setting-rate controller and biodegradable polymers)

IT **Dental materials and appliances**

Medical goods

(cements; hydraulic surgical cements comprising calcium phosphate and setting-rate controller and biodegradable polymers)

IT 127-08-2, Potassium acetate 127-09-3 994-36-5, Sodium citrate 7320-34-5, Potassium pyrophosphate 7487-88-9, Magnesium sulfate, biological studies 7664-93-9, Sulfuric acid, biological studies 7722-88-5 7757-82-6, Sodium sulfate, biological studies 7758-16-9 7778-49-6, Potassium citrate 7778-80-5, Potassium sulfate, biological studies 7790-76-3, Calcium pyrophosphate 10034-76-1, **Calcium sulfate** hemihydrate 13598-36-2D, Phosphonic acid, alkylenebis-derivs., salts 35804-95-6 222719-60-0

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hydraulic surgical cements comprising calcium phosphate and setting-rate controller and biodegradable polymers)

IT 1306-06-5, **Hydroxyapatite**

RL: TEM (Technical or engineered material use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hydraulic surgical cements comprising calcium phosphate and setting-rate controller and biodegradable polymers)

IT **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic acid 9004-65-3, Hydroxypropyl methyl cellulose 9012-36-6, Agarose 9012-76-4, Chitosan 11138-66-2, Xanthan gum 25249-16-5 25322-68-3

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(hydraulic surgical cements comprising calcium phosphate and setting-rate controller and biodegradable polymers)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:222847 HCAPLUS

DOCUMENT NUMBER: 130:257353

TITLE: Inorganic-polymer complexes for the controlled release of compounds including medicinals

INVENTOR(S): Royer, Garfield P.

PATENT ASSIGNEE(S): Buford Biomedical, Inc., USA

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

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|            |    |          |                 |          |
|------------|----|----------|-----------------|----------|
| WO 9915150 | A1 | 19990401 | WO 1998-US19528 | 19980922 |
|------------|----|----------|-----------------|----------|

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

|            |    |          |                 |          |
|------------|----|----------|-----------------|----------|
| US 6391336 | B1 | 20020521 | US 1997-935300  | 19970922 |
| CA 2303884 | AA | 19990401 | CA 1998-2303884 | 19980922 |
| AU 9894925 | A1 | 19990412 | AU 1998-94925   | 19980922 |
| EP 1017364 | A1 | 20000712 | EP 1998-948335  | 19980922 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

|               |    |          |                |          |
|---------------|----|----------|----------------|----------|
| JP 2001517613 | T2 | 20011009 | JP 2000-512521 | 19980922 |
|---------------|----|----------|----------------|----------|

PRIORITY APPLN. INFO.: US 1997-935300 A2 19970922  
WO 1998-US19528 W 19980922

AB This invention relates generally to the prodn. and use of inorg.-polymer complexes for the controlled release of compds. including medicinals. Advantageously, the inorg. used is **calcium sulfate**. CaSO<sub>4</sub> 1000, norfloxacin 50, and iodipamide 110 mg, all finely ground, were mixed and to this mixt. was added 0.6 mL of hyaluronic acid soln. (2 %). The slurry was mixed and loaded into the barrel of a syringe for administration or casting in a mold.

IC ICM A61K009-00  
ICS A61K009-36

CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 5

ST drug delivery matrix **calcium sulfate** hyaluronate

IT **Bone morphogenetic proteins**  
Glycosaminoglycans, biological studies  
**Growth factors, animal**  
Lecithins  
Lipids, biological studies  
Pheromones, animal  
Polynucleotides  
Polyoxyalkylenes, biological studies  
Proteins, general, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(drug delivery systems contg. inorg. compds. and matrix polymers and complexing agents)

IT 50-03-3, Hydrocortisone acetate 50-23-7 57-27-2, Morphine, biological studies 57-88-5, Cholest-5-en-3-ol (3.beta.)-, biological studies 59-46-1, Procaine 87-08-1, Penicillin V 112-38-9, 10-Undecenoic acid 124-07-2, Octanoic acid, biological studies 133-16-4, Chlorprocaine 137-58-6, Lidocaine 140-28-3, Benzathine 147-52-4, Nafcillin 154-21-2, Lincomycin 466-99-9, Hydromorphone 606-17-7, Iodipamide 721-50-6, Prilocaine 1397-89-3, Amphotericin B 1400-61-9, Nystatin 1403-66-3, Gentamicin 1404-90-6, Vancomycin 1406-05-9, Penicillin 1406-11-7, Polymyxin 2203-97-6, Hydrocortisone succinate 6678-14-4 7585-39-9D, .beta.-Cyclodextrin, hydroxypropyl ethers 7778-18-9, **Calcium sulfate** 9002-89-5, Polyvinyl alcohol 9002-98-6 9003-01-4, Polyacrylic acid 9003-39-8, PVP 9003-47-8, Polyvinylpyridine 9004-34-6, Cellulose, biological studies **9004-54-0**, Dextran, biological studies 9004-61-9, Hyaluronic

acid 9005-25-8, Starch, biological studies 9005-32-7, Alginic acid  
 9005-65-6, Polysorbate 80 9007-28-7, Chondroitin sulfate 9042-14-2,  
 Dextran sulfate 10118-90-8, Minocycline 11138-66-2, Xanthan gum  
 15663-27-1, cis-Platin 15686-71-2, Cephalexin 22199-08-2, Silver  
 sulfadiazine 24991-23-9 25322-68-3 25513-46-6, Polyglutamic acid  
 25608-40-6, Polyaspartic acid 25953-19-9, Cefazolin 26063-13-8,  
 Polyaspartic acid 26336-38-9, Polyvinylamine 26913-06-4,  
 Poly[imino(1,2-ethanediyl)] 36637-18-0, Etidocaine 37517-28-5,  
 Amikacin 38396-39-3, Bupivacaine 39831-55-5, Amikacin sulfate  
 52580-78-6, Polymyxin sulfate 53648-55-8, Dezocine 61477-96-1,  
 Piperacillin 64221-86-9, Imipenem 70458-96-7, Norfloxacin  
 81103-11-9, Clarithromycin 85721-33-1, Ciprofloxacin 93106-60-6,  
 Enrofloxacin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (drug delivery systems contg. inorg. compds. and matrix polymers and  
 complexing agents)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L53 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:635680 HCAPLUS

DOCUMENT NUMBER: 129:265493

TITLE: Osteogenic devices and methods of use thereof for  
 repair of bone

INVENTOR(S): Rueger, David C.; Tucker, Marjorie M.; Chang, An-cheng

PATENT ASSIGNEE(S): Creative Biomolecules, Inc., USA

SOURCE: PCT Int. Appl., 147 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.                                                                   | KIND | DATE     | APPLICATION NO. | DATE       |
|------------------------------------------------------------------------------|------|----------|-----------------|------------|
| WO 9841246                                                                   | A2   | 19980924 | WO 1998-US6043  | 19980320   |
| WO 9841246                                                                   | A3   | 19981022 |                 |            |
| W: AU, CA, JP                                                                |      |          |                 |            |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE       |      |          |                 |            |
| US 2001014662                                                                | A1   | 20010816 | US 1997-822186  | 19970320   |
| AU 9867795                                                                   | A1   | 19981012 | AU 1998-67795   | 19980320   |
| AU 751451                                                                    | B2   | 20020815 |                 |            |
| EP 968012                                                                    | A2   | 20000105 | EP 1998-913183  | 19980320   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,<br>IE, FI |      |          |                 |            |
| JP 2001516262                                                                | T2   | 20010925 | JP 1998-540868  | 19980320   |
| PRIORITY APPLN. INFO.:                                                       |      |          | US 1997-822186  | A 19970320 |
|                                                                              |      |          | WO 1998-US6043  | W 19980320 |

AB Disclosed herein are improved osteogenic devices and methods of use  
 thereof for repair of bone and cartilage defects. The devices and methods  
 promote accelerated formation of repair tissue with enhanced stability  
 using less osteogenic protein than devices in the art. Defects  
 susceptible to repair with the instant invention include, but are not  
 limited to crit. size defects, non-crit. size defects, non-union  
 fractures, fractures, osteochondral defects, subchondral defects, and  
 defects resulting from degenerative diseases such as osteochondritis  
 dissecans.

IC ICM A61L027-00  
CC 63-7 (Pharmaceuticals)  
Section cross-reference(s): 2, 3

IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(10; osteogenic devices and methods of use thereof for repair of bone)

IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(11; osteogenic devices and methods of use thereof for repair of bone)

IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(12; osteogenic devices and methods of use thereof for repair of bone)

IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(15; osteogenic devices and methods of use thereof for repair of bone)

IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(16; osteogenic devices and methods of use thereof for repair of bone)

IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(3; osteogenic devices and methods of use thereof for repair of bone)

IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(5; osteogenic devices and methods of use thereof for repair of bone)

IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(6; osteogenic devices and methods of use thereof for repair of bone)

IT **Bone morphogenetic proteins**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(9; osteogenic devices and methods of use thereof for repair of bone)

IT **Growth factors, animal**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF1, growth differentiation factor 1; osteogenic devices and methods of use thereof for repair of bone)

IT **Growth factors, animal**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF10, growth differentiation factor 10; osteogenic devices and methods of use thereof for repair of bone)

IT **Growth factors, animal**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF11, growth differentiation factor 11; osteogenic devices and methods of use thereof for repair of bone)

IT **Growth factors, animal**  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(GDF3, growth differentiation factor 3; osteogenic devices and methods of use thereof for repair of bone)

IT **Growth factors, animal**

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF6, growth differentiation factor 6; osteogenic devices and methods of use thereof for repair of bone)

IT **Growth factors, animal**

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF7, growth differentiation factor 7; osteogenic devices and methods of use thereof for repair of bone)

IT **Growth factors, animal**

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF8, growth differentiation factor 8; osteogenic devices and methods of use thereof for repair of bone)

IT **Growth factors, animal**

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(GDF9, growth differentiation factor 9; osteogenic devices and methods of use thereof for repair of bone)

IT **Bone formation**

(repair; osteogenic devices and methods of use thereof for repair of bone)

IT 69-65-8, Mannitol 1306-06-5, **Hydroxyapatite** 7758-87-4, Tricalcium phosphate 9002-04-4, Thrombin 9004-32-4, Sodium carboxymethylcellulose 9004-34-6D, Cellulose, alkyl derivs., biological studies **9004-54-0**, Dextran, biological studies 9004-62-0, Hydroxyethylcellulose 9004-65-3 9004-67-5, Methylcellulose 9032-42-2, Methylhydroxyethylcellulose  
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(osteogenic devices and methods of use thereof for repair of bone)

L53 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:253359 HCAPLUS

DOCUMENT NUMBER: 120:253359

TITLE: Biocompatible polymer conjugates of natural polymers

INVENTOR(S): Rhee, Woonza; Wallace, Donald G.; Michaels, Alan S.; Burns, Ramon A., Jr.; Fries, Louis; Delustro, Frank; Bentz, Hanne; McCullough, Kimberly; Damani, Ramesh; Berg, Richard A.

PATENT ASSIGNEE(S): Collagen Corp., USA

SOURCE: PCT Int. Appl., 103 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 18

PATENT INFORMATION:

| PATENT NO.                                                         | KIND | DATE     | APPLICATION NO. | DATE     |
|--------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 9401483                                                         | A1   | 19940120 | WO 1993-US6292  | 19930701 |
| W: AU, JP                                                          |      |          |                 |          |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE |      |          |                 |          |
| US 5324775                                                         | A    | 19940628 | US 1992-907518  | 19920702 |

|                                                                       |    |          |                |          |
|-----------------------------------------------------------------------|----|----------|----------------|----------|
| US 5328955                                                            | A  | 19940712 | US 1992-922541 | 19920730 |
| US 5292802                                                            | A  | 19940308 | US 1992-985680 | 19921202 |
| US 5308889                                                            | A  | 19940503 | US 1992-984197 | 19921202 |
| AU 9346620                                                            | A1 | 19940131 | AU 1993-46620  | 19930701 |
| AU 677789                                                             | B2 | 19970508 |                |          |
| EP 648239                                                             | A1 | 19950419 | EP 1993-916926 | 19930701 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE |    |          |                |          |
| JP 08502082                                                           | T2 | 19960305 | JP 1993-503427 | 19930701 |

PRIORITY APPLN. INFO.:

|                |    |          |
|----------------|----|----------|
| US 1992-907518 | A  | 19920702 |
| US 1992-922541 | A  | 19920730 |
| US 1992-984197 | A  | 19921202 |
| US 1992-984933 | A  | 19921202 |
| US 1992-985680 | A  | 19921202 |
| US 1993-25032  | A  | 19930302 |
| US 1988-274071 | B2 | 19881121 |
| US 1989-433441 | A2 | 19891114 |
| WO 1993-US6292 | A  | 19930701 |

AB Non-immunogenic conjugates are formed by covalently binding a biol. inactive, natural polymer or deriv. thereof to synthetic hydrophilic polymers, e.g. PEG, via specific types of chem. bonds. The biocompatible conjugates can be used for soft tissue augmentation and for coating or forming various articles. The compns. may include other components such as liq., pharmaceutically acceptable carriers to form injectable formulations, and/or biol. active proteins such as growth factors or cytokines. A soln. of transforming growth factor .beta.1 (TGF-.beta.1) was added to a soln. of difunctionally activated PEG and the mixt. was allowed to react for 2 min at 17.degree.. To this soln. was added a fibrillar atelopeptide collagen soln. and the resulting mixt. allowed to incubate overnight at ambient temp. to form pellets comprising collagen-PEG-TGF-.beta.1 conjugate. After washing the pellets 6 times with phosphate buffer .apprx.50% of TGF-.beta.1 was retained in the compn.

IC ICM C08G063-48  
ICS C08G063-91; C08H001-00; A61K037-12

CC 63-5 (Pharmaceuticals)  
Section cross-reference(s): 38

IT **Animal growth regulators**  
Glycosaminoglycans, biological studies  
Interferons  
Lymphokines and Cytokines  
RL: BIOL (Biological study)  
(conjugates with synthetic polymers, pharmaceutical compn. contg.)

IT **Animal growth regulators**  
RL: BIOL (Biological study)  
(blood platelet-derived growth factors, AA, conjugates with synthetic polymers, pharmaceutical compn. contg.)

IT **Animal growth regulators**  
RL: BIOL (Biological study)  
(blood platelet-derived growth factors, AB, conjugates with synthetic polymers, pharmaceutical compn. contg.)

IT **Animal growth regulators**  
RL: BIOL (Biological study)  
(blood platelet-derived growth factors, BB, conjugates with synthetic polymers, pharmaceutical compn. contg.)

IT **Animal growth regulators**

- RL: BIOL (Biological study)  
 (bone morphogenetic proteins, conjugates  
 with synthetic polymers, pharmaceutical compn. contg.)
- IT **Animal growth regulators**  
 RL: BIOL (Biological study)  
 (osteogenins, conjugates with synthetic polymers, pharmaceutical compn.  
 contg.)
- IT **Animal growth regulators**  
 RL: BIOL (Biological study)  
 (.beta.-transforming growth  
 factors, conjugates with synthetic and natural polymers,  
 pharmaceutical compn. contg.)
- IT **Animal growth regulators**  
 RL: BIOL (Biological study)  
 (.beta.2-transforming growth  
 factors, conjugates with synthetic and natural polymers,  
 pharmaceutical compn. contg.)
- IT 409-21-2, Silicon carbide, biological studies 1306-06-5,  
**Hydroxyapatite** 7758-87-4, Tricalcium phosphate 9002-84-0, Ptfе  
 RL: BIOL (Biological study)  
 (beads, pharmaceutical compn. contg. conjugates of natural and  
 synthetic polymers and, for repair of bone defects)
- IT **62229-50-9, Epidermal growth factor**  
 RL: BIOL (Biological study)  
 (conjugates with synthetic polymers, pharmaceutical compn. contg.)
- IT 9004-34-6D, Cellulose, ethers, conjugates with synthetic polymers  
**9004-54-0D, Dextran**, conjugates with synthetic polymers  
 9004-61-9D, Hyaluronic acid, conjugates with synthetic polymers  
 9004-62-0D, Hydroxyethyl cellulose, conjugates with synthetic polymers  
 9005-25-8D, Starch, conjugates with synthetic polymers 9061-61-4D, Nerve  
 growth factor, conjugates with synthetic and natural polymers  
 11096-26-7D, Erythropoietin, conjugates with synthetic and natural  
 polymers 12619-70-4D, Cyclodextrin, conjugates with synthetic polymers  
 24967-93-9D, Chondroitin sulfate a, conjugates with synthetic polymers  
 24967-94-0D, Dermatan sulfate, conjugates with synthetic polymers  
 25322-46-7D, Chondroitin sulfate c, conjugates with synthetic polymers  
**61912-98-9D, Insulin-like growth factor**, conjugates with synthetic  
 and natural polymers 62683-29-8D, Colony stimulating factor, conjugates  
 with synthetic and natural polymers 69344-76-9D, Connective  
 tissue-activating peptide I, conjugates with synthetic and natural  
 polymers 106096-92-8D, Acidic fibroblast growth factor, conjugates with  
 synthetic and natural polymers 106096-93-9D, Basic fibroblast growth  
 factor, conjugates with synthetic and natural polymers 111575-54-3D,  
 conjugates with collagen 154467-38-6D, conjugates with collagen  
 154467-39-7  
 RL: BIOL (Biological study)  
 (pharmaceutical compn. contg.)